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1921

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PROGRESSIVE MEDICINE

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES
AND IMPROVEMENTS

IN THE
MEDICAL AND SURGICAL SCIENCES

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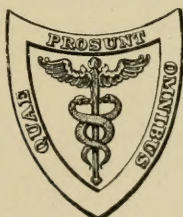
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VOLUME III. SEPTEMBER, 1921

OBSTETRICS—DISEASES OF THE THORAX AND ITS VISCERA, INCLUDING THE HEART
LUNGS AND BLOODVESSELS—DERMATOLOGY AND SYPHILIS—DISEASES
OF THE NERVOUS SYSTEM



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PROGRESSIVE MEDICINE.

SEPTEMBER, 1921.

OBSTETRICS.

BY EDWARD P. DAVIS, M.D.

The Future of Obstetrics as a Specialty. Peterson¹ in the chairman's address read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Meeting of the Association, April, 1920, considered at length the future of obstetrics and also that of gynecology.

In speaking of the training of a specialist in obstetrics, he alludes to one method by which a medical man entering upon general practice may gradually eliminate all medical work, except in the field for which he is best qualified, and in which he has the most interest; many eminent obstetricians in America have achieved distinction in this way. Another method is by graduating from a large medical school and obtaining a position as assistant in the teaching and hospital corps of the medical school and in the clinics devoted to the subject in which he desires to become proficient. There are advantages in both methods for becoming specialists. The man who has experience in general practice gains a broad, general training which is of service in estimating the value of symptoms and their relation to the general health of the particular malady which demands the attention of the specialist. On the other hand one cannot attain operative skill and experience except in clinical work, and such can only be secured in hospital clinics. If this course be carried on indefinitely a specialist in obstetrics and gynecology may not be confined to the comparatively narrow operative field of this specialty, but may join the ever-enlarging company of men who started out to be obstetricians and gynecologists and ended in being general surgeons with a fondness for gynecology. The writer believes that obstetrics and gynecology should be united in medical schools and hospital clinics; if this be not the case, in the near future there will be no specialty of obstetrics and gynecology, as the man who desires to attain operative efficiency will join the larger field of surgery, which will embrace gynecology.

Obstetrical teaching has been deficient and seriously handicapped because of the failure to provide proper facilities for instruction in this

¹ Journal of the American Medical Association, May 15, 1920.

particular branch of medicine. Obstetrical material is expensive to the hospital, as most of the patients can pay nothing and yet demand considerable care. This has led to the building up of out-patient obstetric clinics which are wasteful in clinical material and which teach badly. The writer terms this method a time-wasting and illogical method of instruction, and if the contention be true that by this method students are taught to meet conditions which will pertain in practice, it would be logical to apply this method to the teaching of surgery and medicine. In the tenement houses, practitioners are not always able to send medical and surgical patients to the hospital and must often treat fractures and pneumonia at the patient's homes. The writer believes that obstetricians without adequate training in gynecology and gynecologists without obstetric training are both seriously handicapped; both he terms unfinished products, and neither can afford to reproach or insult the other. Their deficiencies cannot be made good by adding diseases of children or abdominal surgery to their respective fields of labor.

The writer thinks that the future of obstetrics and gynecology depends largely on the policy of the medical schools toward the specialty in the near future; if adequate funds and facilities are provided in the departments of obstetrics and gynecology and the two combined under one head the specialty will flourish and the subjects will be well taught and research work of value will be done. If this be not the case then the reverse will occur, otherwise gynecology will gradually be merged in surgery.

In organizing such a department in the medical school and hospital, opportunity should be given for the student to obtain a living income while acting as a junior teacher. Such a student should obtain equal experience in both branches. With a person so trained, if he goes into practice instead of continuing his academic career he may decide to be a specialist in both branches or devote his time to one division of the specialty. Each student must adjust for himself his hours and methods of work as his work develops. If he is properly educated and trained he will do good work and will add somewhat to the sum of human knowledge.

It is evident that obstetrical specialists must be prepared at any time to resect the intestines and care for the appendix and gall-bladder if such surgery be demanded when the abdomen is opened for pelvic disease. Literary training in these branches is an absolute necessity. To secure actual experience and technical skill in abdominal surgery, arrangements can usually be made for interchange of services during training, to the mutual benefit of members of the surgical and gynecological staff. This interchange of service is a good one in the various branches of a hospital.

The reviewer would call attention to the fact that recent advances in obstetrics and gynecology have been much greater in obstetrics and much more valuable than in gynecology; perhaps the most important subject engaging the attention of the gynecologist is cancer of the female reproductive organs, and gynecologists show no better help for the patient so afflicted at the present time than early and thorough operation,

and even with this and with the supplementary use of radium and the x-ray are results sufficiently satisfactory to lead to the assertion that an important and lasting gain has been made? In prolapse of the generative organs caused by the general relaxation of the fascia of the pelvis, has gynecology provided a thoroughly satisfactory correction by operation? Can the gynecologist relieve by surgery or other treatment a large percentage of cases of sterility caused by disease of the female generative organs?

In direct contrast to this stands the development of delivery by abdominal section, through various methods, which has deprived a contracted pelvis of its pathological importance and provided a prompt and safe relief in accidental separation of the placenta. Many cases of placenta previa, even when the case has been badly handled and the woman has been infected may still be saved by delivery by section with hysterectomy and extraperitoneal treatment of the stump. In puerperal septic infection we have learned in obstetrics the comparative importance of streptococcus infection and infection arising from foci in the woman's body, notably those arising in the intestinal tract. The suffering of labor is now largely controlled by obstetricians, and much of the dread naturally felt by women for parturition has been removed. Postpartum hemorrhage is now prevented or promptly controlled, and death from this cause is rare. While the toxemia of pregnancy in both the early and late months, with or without convulsion, is still an unsolved problem, much has been done to diminish the frequency of this complication and save maternal life when it arises. No man at present can pertain to the title of obstetrician who cannot deal, by abdominal section, with rupture of the uterus, appendicitis or cholecystitis requiring draining of the gall-bladder. It is questioned if in any other branch of medicine so great and decided progress has been made as in obstetrics in the last few years.

The reviewer is in hearty accord with the writer in his condemnation of out-patient obstetric practice; not infrequently the student is taught to do his obstetrical work in the worst manner possible. If surgery and medicine cannot be taught successfully in homes of patients, certainly a condition in which two lives are at stake demands hospital care. The necessity for replacing human life so fearfully wasted in recent years by the World War may afford opportunity for improvement in facilities for the teaching and practice of modern obstetrics.

PREGNANCY.

The Circulatory Apparatus in Pregnancy. On June 15, 1920, before the Obstetrical Society of Vienna was held an interesting discussion of pregnancy and the circulatory apparatus, of which a report is given in the *Zentralblatt f. Gynäkologie*, 1920, No. 39, p. 1092. Fellner drew attention to the fact that there is no anatomical ground for the condition called the "heart of pregnancy." This is an old controversy which resembles that carried on concerning the condition of the heart in goiter and fibroid tumors of the uterus. There are, however, many clinical

symptoms pointing to disordered action of the organs of circulation. Patients complain of labored action of the heart, shortness of breath, sleeplessness and edema; in many cases this results from the pressure of the uterus on the large bloodvessels and on the diaphragm. A certain number of these patients have a disordered action of the thyroid so often seen in pregnancy; such patients suffer from tachycardia, often paroxysmal, excessive perspiration, attacks of syncope, looseness of the bowels, irregular action of the heart, scleroderma and, to some extent, exophthalmos. This condition is probably the result of the pregnancy toxemias. When women have borne a number of children in quick succession the action of the heart is disturbed, and often it is because of some alteration in the heart muscle. In other patients the lesion lies in the vessels. If this fact is remembered one can understand why women who have had heart disease for some time, but preserved good compensation, when pregnancy occurs fail in compensation and suffer sometimes greatly. So women in pregnancy having heart lesions but good compensation often do very badly as soon as the first signs of labor appear because of the influence of labor in producing toxins and their effect upon the vascular system. If one studies cases of heart disease complicating pregnancy he finds there are usually indications that compensation is failing before serious symptoms develop; these should give warning and occasion prompt relief by treatment. In 220 cases treated in Shauta's Clinic the mortality was about 2 per cent, with the loss of half of the children because of abortion or premature labor. For each child surviving in each of these cases and reaching the age of twenty-four years, as a rule two mothers have perished. One must not be content with estimating the actual mortality among these patients as the only result of heart disease. The mother's health is permanently and seriously damaged by such an experience and her duration of life considerably shortened.

Mitral stenosis is recognized as one of the most serious of these lesions, whether it be acquired or congenital. Some would urge that if this condition were present, pregnancy should be terminated whether compensation had begun to fail or was still good. One must not place too much reliance on murmurs in these cases because changes in circulation may produce murmurs without structural alterations. It is difficult to find an explanation for the rapid flow of blood through the heart during pregnancy. The heart itself does not beat with greater than normal rapidity. Investigation has shown that the actual quantity of blood in the vessels of the pregnant woman is increased one-twelfth over that of the non-pregnant. This accounts for the partial dilatation of the heart often seen during pregnancy, but if circulation is quickened this dilatation may not occur. In the puerperal period heart murmurs are not uncommon soon after labor, but as soon as the patient has rested and become accustomed to lying quietly these murmurs should disappear; but, as a matter of fact, they do not. The probabilities are that these murmurs are caused by temporary dilatation of the heart.

Recurrent endocarditis is a grave complication of pregnancy. Of 5 women admitted to the clinic with this condition 3 died, of whom 2 were

in the sixth month. In very early pregnancy it is well to interrupt at once, and in the later months, if possible, the patient should not be disturbed. When there is disease of the thyroid the gravity of the complication is increased. Of 10 patients 2 died; in 4 pregnancy was interrupted and 1 patient aborted; thus in 5 pregnancies there were 2 deaths. As a rule, even though there is good heart compensation, a thyroid condition of importance calls for the interruption of pregnancy.

Should birth be undertaken the question arises which is the more dangerous, a slow and gradual birth or a rapid delivery? The writer believes that it is safer that the uterus be emptied slowly and that the heart accommodates itself better in this way to the changed conditions. Theoretically the strain of labor pains and uterine contractions are better avoided; on the other hand in Cesarean section there is a marked fall in blood-pressure at the moment after the child is delivered, which does not occur in spontaneous birth; this is also seen in birth by forceps and by version, and this fall is usually followed by collapse, and cases are on record in which death has been the result. Further study in the application of Cesarean section in these cases is indicated.

The question of sterilization of these patients is of importance. In cases in which it is evident that each future pregnancy must be terminated artificially the writer is in favor of sterilization by hysterectomy in the early months of gestation. This should be done in cases of mitral stenosis, especially if complicated with nephritis or goiter, and in all cases in which in previous pregnancies the patient's life has been threatened during pregnancy or labor and also when it is evident that the heart muscle is badly diseased.

Holban raises the question, When should pregnancy in these cases be interrupted? The majority of opinion would favor this course if mitral stenosis is present, but if compensation is good this may not be necessary. As a rule, pregnancy is to be interrupted only when the first signs and symptoms of failure of compensation develop. Clinical observation shows that if the heart does not accommodate itself to the pregnant condition, compensation fails early in pregnancy, and in these cases pregnancy must promptly end, for such a patient cannot endure labor. He has also observed the fatal effect of hemorrhage on pregnant women having diseased hearts. In view of this he would interrupt pregnancy if compensation began to fail. Should a patient having a chronic heart lesion fail once only in compensation it does not follow that a future pregnancy is absolutely contraindicated—each case must be studied upon the merits of the individual. In one case of mitral insufficiency and stenosis it was necessary to interrupt pregnancy because compensation failed; two years later pregnancy recurred, and at the patient's earnest desire she was put under strict régime and carried through to the end of pregnancy in normal labor.

In labor every effort must be made to spare the patient all undue strain and suffering. During the period of dilatation, narcotics should be freely given; when the stage of expulsion is reached it should be shortened by operative assistance. A case is recalled in which a patient with severe heart lesion was allowed to pass through the early months

without interruption; during labor with strong pains she suddenly developed edema of the lungs and cyanosis. She was rapidly delivered by dilating the cervix and placed under an anesthetic with morphine and the head was delivered by the high application of forceps; fortunately a good result followed.

Bauer drew attention to diseased conditions of the media of the blood-vessels complicating these cases. This condition is most often found in vessels of average size and where the circulation is failing. These resemble cases of arteriosclerosis. Other cases are seen in which a paralysis of the vasomotors exist, like that observed in acute infectious diseases. These patients suffer not only from anemia but at the time of labor from venous congestion and failure in the pulmonary circulation.

The influence of the ductless glands must not be forgotten in studying these cases. Thus one sees tetany, acromegaly, disturbance of the suprarenals and thyroid. In these cases the writer did not believe in waiting in pregnancy until circulation was on the point of serious failure. Each case should be carefully studied and such a course of action selected as would give to the individual case the best chances. The many factors which have to do with the life of the individual require careful study and close analysis.

Weibel has studied 208 pregnant women who had disease of the heart; of these 52 were in labor (among them were 24 cases of mitral stenosis, 12 with good compensation and 12 with bad); 28 cases of other heart lesions (17 with good compensation and 11 with bad). In the 12 cases of mitral stenosis with bad compensation 4 only required instrumental assistance in labor; 1 of these cases with bad compensation died three days after labor with purulent peritonitis. There were 156 cases of pregnant women with heart lesions admitted to the clinic, and in most of them the question of interruption of pregnancy was at once considered. Of these, 79 cases were mitral stenosis (28 with good compensation and 51 with bad) and 77 cases of other lesions (38 with good compensation and 39 with bad). About half of all pregnant women having valvular disease of the heart have mitral stenosis. This is accounted for in hospital statistics by the fact that more of these patients are sent to hospitals with the idea of having the pregnancy interrupted than with any other kind of heart disease. Among these there were 38 in whom pregnancy was interrupted, 28 with mitral stenosis, 7 with good and 21 with bad compensation, and 10 cases of other lesions, 1 with good compensation and 9 with bad. One case of mitral stenosis with good compensation had pregnancy interrupted at two months, followed by death fourteen days later from heart failure. Another patient at six months received an injection in the spinal canal of tropococain 0.06, followed by sudden death. The others made good recoveries. When one considers the ultimate result of patients in whom pregnancy was not interrupted they find 2 cases dying of what was a purely cardiac cause: 1 had bad compensation, aortic insufficiency and goiter, the general condition being so bad as to forbid operation; she died undelivered twelve hours after admission. The second patient with mitral stenosis received medical treatment twenty-three days, finally giving birth to a macerated

child and dying suddenly two hours afterward. Two patients with bad compensation and mitral and aortic disease died of hemorrhage from deep lacerations of the cervix produced in emptying the uterus. Another patient seven months pregnant had syphilis of the aorta and died suddenly at the end of pregnancy; another, aged forty years, a multipara, died in the last month of pregnancy from sudden failure of the action of the heart with evidence of hypoplasia of the aorta. Each case must be studied on its merits and one cannot make a hard-and-fast rule to interrupt every pregnancy having a given heart lesion. The writer favors rapid delivery by dilatation and curetting in the early months, and in the later months selecting vaginal or abdominal section in accordance with the nature of each case.

The question of sterilization must be considered, and oftentimes this must be carried out in the first half of pregnancy. This can be done through the vagina and in the second half through an abdominal incision. Inhalation anesthesia is forbidden in these cases, and anesthesia by infiltration, while possible, is not entirely satisfactory; sacral or lumbar anesthesia is sometimes uncertain and dangerous. On the whole, however, the writer favors the injection of narcotics into the spinal column.

Hocksinger drew attention to congenital disease of the heart complicating pregnancy. From the clinical standpoint he would divide the cases into those with cyanosis and those without. Pregnancy exerts a very depressing and dangerous influence upon the first class of patients. Those without cyanosis often bear pregnancy well and much resemble cases of mitral insufficiency with good compensation. He draws attention to those cases called "blue babies," in which there is congenital lesion of the heart and cyanosis; however, few of them live to or beyond the age of puberty, and hence are rarely seen in the pregnant condition. In cases of congenital heart lesion with cyanosis it is sometimes observed that the cyanosis disappears after labor only to appear later in life when the patient has a serious illness. However, in such a case, should any condition arise during pregnancy throwing additional strain upon the heart and should cyanosis grow worse, pregnancy must at once be interrupted. The lesion present in most congenital cases is stenosis of the pulmonary artery with some defect in the septum of the heart. Four-fifths of all congenital cardiac cases have these lesions. This cyanosis results from a mixing of venous and arterial blood in the chambers of the heart through a defective partition and through the backing up of blood in the right heart and veins because of the stenosis in the pulmonary artery. So long as the heart muscle remains strong the circulation can still go on in spite of these defects. The cyanosis does not increase and the patient feels usually well. When extra strain is thrown upon the heart the right ventricle appears insufficient and dilates; there is stoppage of circulation in the right heart and in the veins of the body, and the left ventricle is overfilled with venous blood through the defect in the septum. The aorta and artery become similarly burdened and there results a venous mixture of blood in the arteries with constant congestion in the veins and increasing congestion in the lungs. Cyanosis then becomes extreme. The writer uses the term paleness of the skin

as contrasted to cyanosis in the ordinary sense of the word. This he considers the gravest symptom which can develop in such a case; sudden death readily occurs from rapid dilatation and failure of the heart muscle. In two cases of this sort which the writer observed from childhood both died in the second third of pregnancy with general bluish discoloration of the skin before any attempt had been made to end the pregnancy. It follows from these facts that a case of congenital heart lesion with permanent bluish discoloration of the skin, complicated by pregnancy, should be promptly interrupted. A simple defect in the wall of the heart may cause no complication if compensation is good; some of these patients have loud systolic murmurs, louder than usual in the last weeks of pregnancy; in these cases cyanosis is absent. The writer mentions a woman born with such a defect who became an opera singer, married and gave birth to two children, and in her professional and domestic life suffered no inconvenience and had no bad symptoms.

Another patient had a congenital defect in the septum with persistent loud murmur; she came to puberty safely, later married and gave birth to two children without difficulty. Evidently the diagnosis between an uncomplicated defect in the cardiac septum and a complicated congenital lesion is an important one. Most of these congenital defect cases are diagnosticated mitral insufficiency; they do not have a systolic murmur which follows hypertrophy of the right ventricle nor accentuation of the second pulmonary tone which is often seen in other forms of the disease. If these cases are carefully studied it is usually possible to make a diagnosis of mitral insufficiency and septum defect. The intensity of the systolic murmur in the third left intercostal space underneath the attachment of the third left costal cartilage to the sternum is of importance, and also the failure of the murmur over the apex and often a failure to detect a thrill over the area of the heart. Sometimes all symptoms vanish during pregnancy, and the physician may think he is dealing with a simple case of mitral insufficiency. The decision to interrupt pregnancy must not be based upon one or two symptoms but on the general condition of the patient. The fact remains that when pregnancy is complicated by congenital heart lesions it must be interrupted when permanent paleness of the skin is present or develops; but if this important symptom is absent the pregnancy may go on.

In closing the discussion, various operators raised the question of anesthesia by infiltration in abdominal section with sterilization. It has been observed that the parietal peritoneum is sensitive, and this seems a grave objection to this method. Some were afraid to give narcotics before operation, believing that they depress the circulation; but, unfortunately, anesthesia by spinal injection is equally dangerous. Attention was drawn to the fact that for vaginal section anesthesia by infiltration would be very difficult. The choice in spinal anesthesia was the fact that results were obtained by the smallest possible quantity of poisonous substance in the circulation. If this method is chosen care must be taken not to put the patient in the Trendelenburg posture.

The reviewer has recently had occasion to deliver a patient, aged

twenty-six years, in her second pregnancy, who had suffered many years with aortic insufficiency and mitral stenosis. In the early months of cardiac disease she had borne a child successfully through the vagina. Husband and wife requested sterilization, and in view of the cardiac condition and the fact that the patient could not be very comfortably cared for it was determined to terminate pregnancy by section with sterilization; anesthesia with novocain and adrenalin was given; the abdominal wall was freely infiltrated and then the parietal peritoneum. Section was painless and opening of the uterus occasioned little disturbance. To guard against the shock following the fall in blood-pressure upon emptying the uterus, the skin of one arm was infiltrated, and intravenous saline transfusion was performed while the operation was in progress. The broad ligament was found to be sensitive, and this was in turn infiltrated; sterilization was done by completely removing each Fallopian tube. The layers of the broad ligament were drawn together by continuous catgut suture. The operation proceeded smoothly and the patient made a good recovery. The child weighed over six pounds and breathed readily, and was apparently in good condition, but died twenty hours after delivery with cyanosis. Autopsy revealed no adequate cause for death; there was a clot over the cerebral cortex, but this was not of sufficient size to bring about the fatal termination. As the child had not been subjected to any violence the occurrence of this clot was not explained.

Lingual Struma Complicating Pregnancy. Ruble² reviews, in the beginning of his paper, the literature upon the subject and calls attention to the fact that the first case of lingual struma on record was reported in the year 1869 by Hickmann.³ After him Butlin, in a book on *Diseases of the Tongue*, characterized the tumor as adenoma. In 1912 Walter had collected 70 cases, and in 1914 Asch reported 95 cases which he had collected from the literature. A description of these cases is found in works upon pathology, surgery and laryngology. The writer observed a case in the clinic at Bern in the year 1918; the situation of the tumor was at the root of the tongue. The thyroid gland, as ordinarily described, consists of three portions: the middle arises from the epithelia in the region of the jaws, two lateral portions develop afterward, and all can be made out in a microscopic study of the embryo by the seventh week. The middle portion occupies the site of the ductus thyroglossus, and usually this middle portion atrophies and disappears. When it seems to blend with the epithelia of the floor of the mouth it forms what is later called a foramen cecum. If thyroid tissue remains in this region and later becomes degenerate, it forms the tumor in question. It is known that in cases of thyroid disease tetany develops if all of the gland is removed, but the characteristic epithelial bodies have not been detected in these lingual struma; so if this tumor is removed tetany does not develop, although Asch reports his case of lingual struma where tetany did develop after total extirpation and epithelial bodies were present in the tumor. Most of these tumors have developed in women.

² Monatschrift f. Geburtshülfe, November, 1920, v, 295, No. 52.

³ Pathological Transactions, vol. xx.

It is recognized that the thyroid has an important function in the health of women, and hence it is not strange that these tumors should occur in the female sex.

The case reported is as follows: The patient, aged twenty-eight years, was a primipara who had had no abortion. The history showed that in childhood the patient had a nasal voice. She seemed to have no difficulty in breathing and so had no medical attention paid to this circumstance. When menstruation developed there was difficulty in breathing which increased at each menstrual period; anemia also developed, but aside from this the patient had had no illness. Menstruation began at eighteen years, was regular and lasted four or five days, with a scanty discharge. The patient suffered from headache and cramp-like pains in the abdomen between menstrual periods. This persisted until she became pregnant. The early months of pregnancy were characterized by no special complication. In the second half of pregnancy she began to complain of pain in the neck, dyspnea on the slightest exertion and when she tried to use the voice. Toward the end of pregnancy her suffering became much greater and a physician was consulted. Upon entering the hospital there was no deformity of the skeleton and the sexual organs seemed fairly developed. The fundus of the uterus was between the umbilicus and the symphysis; fetal movements could be made out, but the child had not descended into the pelvis; fetal heart sounds could be heard near the umbilicus. The pelvis showed no signs of rickets. The pubic arch was very narrow, the symphysis high and it was impossible to accurately palpate the lateral pelvic wall. The promontory of the sacrum was reached with the greatest difficulty by rectal examination. The pelvis measured: Spines 19 cm., crests 24 cm., trochanters 27 cm., external conjugate 10.5 cm., true conjugate 8 cm. The cervix was not obliterated but the external os was closed. The patient's blood showed 65 to 70 per cent hemoglobin. The urine showed a trace of albumin, but no sugar. Upon examining the neck the larynx could be plainly made out, but no thyroid tissue could be found in its usual location; beneath the chin on both sides and extending posteriorly a tumor could be felt. The consistency was firm, but the tumor was not attached to the skin; the anterior portion of the tongue was normal; the posterior portion of the mouth was greatly encroached upon by a tumor having its origin at the base of the tongue and extending forward upon the right side. The tumor was covered by dark red mucous membrane containing numerous distended veins. The tumor almost blocked the fauces, so that breathing and phonation were accomplished with difficulty.

When labor pains began the patient became much distressed, dyspnea and cyanosis developed and the patient could only speak with great effort and pain. The tumor practically filled the fauces and the finger could not be passed beyond the tumor. Cesarean section was performed under local anesthesia, and no difficulty was found in extracting a living child and closing the uterine wound and abdomen. Preparations had been made to do a tracheotomy, but this was not necessary, and on the following day the condition had decidedly improved: cyanosis had dis-

appeared, the patient could speak much better and in the few days which followed the patient passed through a mild bronchopneumonia. The Cesarean wound healed completely and the patient returned practically to the condition in which she had been before conception. The tumor had grown so small that she could breathe freely, but the speech still retained its nasal character.

In the early months of pregnancy should a patient develop threatening symptoms because of lingual struma a choice must be made between therapeutic abortion and surgical operation upon the tumor. When viability has been reached there is no question but that interruption of pregnancy should be the choice. If the patient comes into spontaneous labor suffering from this condition and symptoms are threatening the labor must be terminated as soon as possible. The question of sterilization must also be considered in the treatment of these patients. A woman passing through such an experience should not be allowed to nurse her child.

The Amniotic Liquid During Pregnancy. Shriener,⁴ draws attention to the difference in the puerperal period in the cases of patients who have been subjected to vaginal examination and those who have not been so treated. His observations were made in the Frankfort Clinic. It is the custom of the clinic, so far as possible, to conduct labor by external examinations and also by rectal examinations. He considers it of importance to make bacteriological examinations of the amniotic liquid, which is done in the clinic, at each Cesarean section. At this operation it is possible to infect the abdominal wound by amniotic liquid, and should suppuration in the wound occur it would seem to indicate that bacteria in the amniotic liquid were the cause of the infection. Whether these bacteria have gained access to the uterus because of vaginal examination is a question of considerable interest.

In 169 transperitoneal operations there were 29 in which the classical transperitoneal with fundal incision was made and 140 in which transperitoneal cervical incision was practised. Ten of these patients died before the abdominal wound could have healed; none of these were from a cause connected with the condition of the genital tract, but all from some illness which rendered necessary termination of labor by Cesarean section. Of the 159 patients recovering, 115 had healing of the abdominal wound by first intention and 44 by second intention. There were 56 cases in which bacteriological examinations were not carried out with sufficient thoroughness to make them available for study. It was the purpose of the writer to study the effects of bacteria which gained access to the amniotic liquid through vaginal examination made during labor or pregnancy and which were conveyed to the wound in the abdominal wall at operation. The cases are divided then into those in which amniotic liquid was found sterile and those in which the abdominal wound healed by second intention, but which did not show in the wound the same bacteria or similar bacteria to those found in the amniotic liquid of the same patient. It is interesting to observe whether the

⁴ Monatschrift f. Geburtshülfe, 1920, iii, 156, No. 53.

secretion of the wound like an abdominal wound could effectually destroy bacteria arising from the genital tract, and 29 cases were observed in which the abdominal wound healed by first intention in which the amniotic liquid contained bacteria, 15 cases in which the abdominal wound healed by second intention, and the same bacteria were found in the amniotic liquid and in the wound. By comparison of those patients examined and not examined it was found that there was a difference of 24 per cent against those subjected to vaginal examination during labor as compared to those who were examined by external or rectal examination. It is thought impossible, in spite of antiseptics and rubber gloves, to make vaginal examinations without carrying bacteria from the perineum and vulva into the vagina.

Allusion is made to the result obtained by Jaegge, a Swiss physician, who found that in cases of spontaneous labor examined through the vagina during labor, 11.6 per cent had a temperature above 100°, while a similar number of patients having spontaneous labor without lacerations, but without such examinations, had only 6.4 per cent in which the temperature rose above 100.° F.

Protein Food and Blood-pressure. It has long been believed that protein food produces a decided increase in blood-pressure. As blood-pressure is one of the most valuable signs in estimating the condition of the pregnant patient, any knowledge bearing upon this point is of practical interest to the obstetrician.

In the *American Journal of the Medical Sciences*, December, 1920, Mosenthal has studied the blood-pressure of patients upon a diet practically without protein and those in whom a considerable quantity of protein was allowed. These patients were kept in bed for several days to bring about a relaxation of the arterial system through rest. It was found that it is exceptional for a low protein diet to diminish blood-pressure or a high protein to raise it. There was one patient, however, extremely ill, with great impairment of renal function and in a state of undernutrition, in which any attempt to increase the amount of protein in the food produced increase of blood-pressure and uremic symptoms; however, in this case, a second period of low protein-feeding failed to bring the blood-pressure to the low level previously obtained. A low protein diet lessened the blood-urea nitrogen, but this seemed to have no effect upon the blood-pressure. Changes in the caloric value of the diet, for a short time at least, did not influence the blood-pressure.

The researches of Benedict show that by underfeeding healthy young persons the blood-pressure can be reduced and that a secondary anemia develops. It seems probable that a subcaloric mixed diet if continued for a considerable time would benefit a case of high tension. Diet should be regulated by hemoglobin content of the blood, which should not fall below 85 per cent.

So far as the management of pregnant patients is concerned we have long known that the percentage of hemoglobin is of great value; we have also observed that it is impossible to materially influence the condition of the pregnant patient by brief change in the diet. As the writer indicates, to obtain a considerable change in a patient's condition the diet and hygiene must be carefully adjusted for a considerable period of time.

Pregnancy Complicated by Benign Decidual Tumors. Nichols⁵ reports 7 cases in which decidual tumors developed during pregnancy and 2 cases in which deciduomata developed after the birth of the child. These tumors consist of normal decidua, its stroma and other portions mingled in varying proportions. An exaggeration in the tendency to glandular proliferation in the normal decidua may result in the development of adenomatous tumor.

An exclusively decidual tumor should contain little or no trace of chorionic structures. Growths consisting of a mixture of chorionic and decidual elements are classed as placental polyps. What is known as the decidual reaction is the change in the non-pregnant endometrium which follows conception. A previously existing uterine tumor may during pregnancy undergo decidual transformation. It is often difficult to determine whether the decidual tumor first developed during pregnancy or whether it is a manifestation of a previously existing growth. Overgrowth of the decidual tumor may form a tumor which may become separated and expelled from the uterus as a fleshy mass with a central cavity. Some would call a placental polyp a decidual tumor, especially if it develops after abortion or labor. In the case of decidual tumor originating before the birth of a child the writer observed two in which the patient aborted and in which the tumor was supposed to be a polyp, but examination showed the greater part of its substance to be decidua. Other cases from Stolper's records show a tumor projecting from the os uteri which was removed, and on examination it was found to consist largely of decidual cells. Other cases reported by Hitschman proved to be adenoma originating from the spongy portion of the decidua and becoming detached during labor. In other cases reported from a Russian hospital two fibroid tumors were found in the uterine muscular substance. Hysterectomy was performed with recovery. Both of the tumors had undergone decidual change.

In one of Maier's cases a woman expelled prematurely a fetus followed by a placenta and a tumor, the tumor being delivered first and the fetus and placenta a half-hour later. The tumor consisted of decidua and the woman afterward developed carcinoma of the uterus. Another patient expelled a tumor which was composed of decidua developing from a chronically inflamed endometrium.

In the 2 cases in which these tumors were expelled after the birth of the child, in 1 reported by Klotz, two years after the birth of the child, the patient suffered from profuse uterine hemorrhage, and examination showed an oval bleeding tumor attached by a broad pedicle to the posterior uterine wall; this was removed and on examination found to be composed of early decidual tissue. The tumor was thought to be an abortive placenta.

Kustner had a patient, aged forty years, who had an abortion at between the second and third months, discharging a fetal and placental mass. There was continuous bleeding, for which operation was done and two tumorous projecting masses were removed from the wall of the uterus; the bleeding stopped and recovery followed.

⁵ American Journal of the Medical Sciences, November, 1920.

These tumors had evidence of the villi of the chorion, which proved that they were connected with the patient's pregnancy. Tumors exhibiting decidual characteristics may develop during pregnancy either as polyps protruding from the os or intra-uterine tumors found at labor. On microscopic study they resemble epithelioma or endothelioma. They are, however, benign and do not indicate the necessity for radical operation. When one can recognize the decidual character of such a polyp it shows that pregnancy is or has very recently been present.

Blood Transfusion During Pregnancy. Doderlein⁶ has had excellent results where there has been extensive hemorrhage during pregnancy into the abdominal cavity by removing the blood from the abdomen, filtering it through gauze and mixing it with 1 per cent solution of citrate of sodium in the proportion of 3 to 2 and injecting it at body temperature into a vein. The internal spermatic vein is considered best for this purpose.

The direct transfusion of blood is described by Oehlecker,⁷ he uses a syringe with two cannulæ which are inserted into a vein. The apparatus is filled with a solution of sodium nitrate and sodium chloride, emptied and then filled with blood so that the amount taken can be known. Experience shows that from 40 to 1000 cc can be successfully used, and the apparatus has been employed for twenty times with good results.

The effect of transfusion upon the blood is illustrated by Huck.⁸ The recipient of the blood shows increased hemoglobin and red blood cells. The question arises whether it is better to give a large quantity at one transfusion with comparatively long intervals or small quantities with repeated transfusion. After a careful study of twenty cases the writer concludes there is no constant and similar effect produced by transfusion and that the mechanical effect of introducing a definite quantity of blood cannot be recognized; what transfusion does is to produce a biological effect in the increase of red blood corpuscles.

Pregnancy and Syphilis. Loeser⁹ has studied the diffusion of syphilis among women, especially since the World War. In 1913 in 39,806 labors there were born 1.5 per cent of children having congenital syphilis. When the use of the Wassermann reaction began in 1917 in three of the large clinics of Germany 3.9 per cent. of congenital syphilis was found. To each 1,000,000 children 39,000 were born syphilitic. The writer believes that these statistics give a low percentage. He alludes to uniform employment of the Wassermann reaction at each case of labor, taking the blood which has accumulated behind the placenta in the uterus.

In discussing this paper obstetricians from Bohemia and portions of Germany spoke of the tremendous increase of syphilis during and since the war.

Encephalitis Lethargica and Pregnancy. Kreiss¹⁰ describes two cases of encephalitis lethargica complicating pregnancy. The first was in her second pregnancy, when she had grippe with a high fever and lung

⁶ Deutsche med. Wehnschrift, 1920, No. 17.

⁷ Zentralblatt f. Gynäkologie, 1920, No. 48.

⁹ Ibid., No. 44, p. 1253.

⁸ Ibid., No. 48.

¹⁰ Ibid., No. 43.

symptoms. There was great restlessness and exaggerated sensations when the temperature was highest. The fall in temperature was accompanied by intense stupor. On examining the patient she was found badly nourished, lying with eyes closed and not responding to voice or touch. There were slight choreic movements of the hands and twitching of the face. The pupils were unequal, although they reacted to light; on the right side slight facial paralysis, ophthalmos and pupil reflex greatly increased. The foot- and ankle-clonus were much increased. There was hyperesthesia over the whole body, but contractions of the uterus could not be made out. The child's heart sounds were normal. The urine contained a small quantity of albumin. The patient remained in the condition of stupor with intense headache. When labor developed with convulsions, between the convulsions the patient remained unconscious. As labor made no progress the patient was delivered by section. The child was feeble and died an hour after its birth. The quantity of albumin rose to 4 per cent., pulse tension 110 and the continuation of unconsciousness. Twitching continued for three days longer. The patient had a subnormal temperature, the quantity of albumin in the urine slowly decreased and after some days the patient's symptoms finally cleared up.

The second patient was a primipara who had been ill for three weeks with gripe with a subnormal temperature. She was taken with unconsciousness, choreic movements and twitching of the face. There was moderate hemorrhage from the genital organs. As the patient was in early pregnancy the uterus was emptied of its contents. The patient passed through a period of unconsciousness, twitching and violent headache, which finally cleared up in about two weeks, the headache persisting.

Similar cases of encephalitis lethargica are reported by Dimetz in Vienna, Gerstmann in Vienna and Couvelaire and Trillet in Paris. It is interesting to note that choreiform movements, restlessness, delirium, violent headache, unequal pupils and exaggerated reflexes are reported by these various observers in this condition.

Latent Syphilis in Pregnancy. At a recent meeting of the Section on Obstetrics of the Royal Society of Medicine, Hendri¹¹ gave the results of his study of 94 pregnancies in which there were 3 with no active clinical signs or symptoms of syphilis apart from the effect on the pregnancy. The diagnosis rested on the clinical evidence, on the laboratory evidence resulting from the examination of specimens and the Wassermann reaction. Clinical evidence had been proved to be unreliable, and in his experience the presence of spirochetes and changes in the various organs were generally considered reliable evidence of syphilis. In his experience their absence is usually reliable. It is difficult to obtain conclusive evidence of syphilis in early abortion, nor is there agreement as to what constitutes the syphilitic lesion of the placenta. He had made a Wassermann test in 348 cases—173 positive and 175 negative. There were 7 cases in which the mother gave a negative reaction and the fetus

¹¹ British Medical Journal, 1920, No. 783.

a positive reaction. The clinical result showed the benefit of treatment when a suspicion of syphilis was present. Thus in 43 cases that had no treatment 7 infants survived the first weeks of life; in 40 cases treated during pregnancy 29 infants survived. In 11 cases treated as soon as pregnancy had been diagnosed all the infants lived. He preferred mercury with chalk to salvarsan, and had found so-called gray oil in some cases useful.

In discussion, Rouch believed that healthy children were born when syphilitic mothers were treated with mercury if treatment was begun at the third month, and this treatment must be repeated in subsequent pregnancies.

The dictum of latent syphilis could be explained in various ways: spirochetes may be broken up into granules, and these may remain inactive and latent for varying periods. Ferments develop, but are, under ordinary circumstances, neutralized, and thus mother and fetus avoid toxemia. It is thought that chorionic ferments can destroy spirochetes and break them up into granules. The continued action of these ferments upon the granules render them latent and inactive and may destroy them. After pregnancy, when these ferments cease to be present in the mother and the child, syphilis may develop. The success or failure of this process may depend upon the virulence of the infection which tends to diminish with each pregnancy, and the source of the infection, whether from the mother when infection would be continually present during pregnancy or from the father when a single infection would occur, and in such a case might be more easily controlled by the ferments. If the granules from the spirochetes remain inactive and the mature organisms are absent the Wassermann reaction from mother and child may be negative.

It is thought that these statements explain the negative Wassermann reaction in infected mothers and their children. In the absence of mature spirochetes in abortion of syphilitic mothers, infection from the semen; the birth of intervening healthy children and Colles's law; when treatment is begun late in pregnancy and is successful it can only be in cases in which the spirochetes have been rendered latent; and in order to accomplish this treatment must be continued in one or both parents and in the child for some time.

Adams gave the results in a series of cases which had been followed after one year's treatment had been carried out in both antenatal and postnatal syphilis. He believes that one year is too short a period in which to bring the treatment of antenatal and postnatal syphilis to perfection, and he does not believe that one could form an accurate idea of the results of treatment until mothers and infants had been under observation for at least two years. Each year the percentage of babies born with a negative Wassermann has increased, and this he believes was the result of more active treatment given to the mothers before confinement and also to the more general use of salvarsan. He looks forward with confidence to the time when the loss of infant life from syphilis will be almost *nil*.

Most of the patients came under observation at about the sixth

month of pregnancy, having been sent with a diagnosis of syphilis made on clinical evidence or from Wassermann reaction. Some had already been treated with mercury and arsenic and showed no definite lesions; others received no treatment whatever; all were practically in the secondary stage of syphilis. In the last two years only one stillbirth and one death followed syphilis in the cases treated. His experience has been that if the mother's Wassermann could be brought down to a negative or doubtful result at the time of her confinement that the baby would be born negative and show no signs of syphilis. If the mother was positive or strongly positive the baby would probably be positive also, and often vigorous antisyphilitic treatment must be begun at once. In a case at present under observation a definite history was obtained that infection took place at about the seventh month and no treatment was given before confinement. At birth the baby had a negative Wassermann reaction, although the mother had syphilis and a strongly positive Wassermann test. None of the babies born with negative reaction had since become positive or developed signs of syphilis, although many had no treatment except from the drugs absorbed through the mother's milk. It might be said in general that pregnant women with syphilis, whether active or latent, if treated for three or four months before confinement would probably be delivered of a healthy child at full term.

The statistics of this interesting series went back over three years, each year beginning on September 1 and ending on August 31. Ninety-five women in the three years were admitted with syphilis. Of the babies born alive 21 had a positive Wassermann reaction and 63 a negative reaction. Four in three years had died of syphilis and 6 in the three years were stillborn. During the three years there were no deaths among the mothers from syphilis.

Gibbs had been accustomed to treat children born of syphilitic mothers, but apparently healthy, by mercury for three years after birth. He did not think it necessary to give salvarsan to infants having no clinical signs of syphilis and negative Wassermann reaction, although the mother may have been syphilitic. He would, however, treat all infants showing signs of infection with salvarsan by the intravenous method, either through the external jugular vein or the anterior fontanelle, and the latter method he found especially useful. He considers it important to give the mother during lactation a full course of salvarsan, and in these cases it is interesting to see the weight of the child increase.

In 100 cases of syphilis during pregnancy 87 showed secondary lesions, 7 had primary lesions only and 1 had tertiary lesions. In 95 per cent of the cases, therefore, the syphilis had not been latent but active. In 84 per cent the Wassermann test was positive, and in 85 per cent of these pregnancy had gone to full term. Eighty-six per cent of the children had been normal at birth, 5 per cent showed syphilitic lesions and 5 per cent showed a wizened appearance, but no signs of syphilis. Of the children born to these mothers 97 per cent gave negative Wassermann reaction and the 3 per cent that were at first positive soon became negative if treated.

Holland quoted the statistics of the Commissioner on Venereal Diseases that 50 per cent of fetal deaths were due to syphilis, and this he believes is an exaggeration. He had examined 300 dead fetuses and found spirochetes in only 37. He endeavored to ascertain what were the most reliable secondary attributes of syphilis in the infants apart from the discovery of spirochetes, and found them to be as follows:

1. The existence of chondro-epiphysitis.
2. Presence of a large spleen or liver.
3. Signs in the placenta indicating syphilis.

In the 37 cases of fetal syphilis only 6 mothers showed clinical evidence of the disease and the other 31 gave a positive Wassermann reaction.

Walker drew attention to the fact that in his belief there is overwhelming evidence that organisms of syphilis might exist in some other form than the spirochetes. This has been shown by examination of syphilitic men. The same observation would apply to the fetus and might explain the failure to find spirochetes in syphilitic abortions. He did not believe that there was direct evidence that the ferments of the chorion could inhibit the spirochetes. As these germs can now be grown in culture it would be possible to test the action of chorionic ferments on them. He believes that the lipoids of the placenta had a strong protecting action against the infecting germs. He believes it would be difficult to obtain reliable statistics as to the frequency of a negative Wassermann reaction in syphilitic pregnant women.

In 226 women in a maternity clinic at Buenos Ayres having clinical signs suspicious of syphilis, 116 had given negative Wassermann reaction. It was difficult to be sure that all of these suspicious cases were actually syphilitic, especially when one remembers that these figures come from a country in which it might be said that a patient was considered syphilitic until he had proved that he was not.

Williams had studied stillborn children with x-rays to determine whether this method could assist in the diagnosis of syphilis. About 15 per cent of the cases showed thickening of the epiphysial line characteristic of chondro-epiphysitis.

In the conclusion of the discussion it was estimated that from 20 to 25 per cent of fetal deaths were due to syphilis, which would bring an annual mortality of 27,000.

The Development of Changes in the Blood in Cases in which Transfusion may be Practiced. Zimmermann¹² has studied the development of isoagglutinin and isohemolysins in cases in which blood transfusion is employed. In studying the literature he found 576 cases of blood transfusion in parturient patients in which hemolysis developed in 1.7 per cent. Among these patients death occurred 27 times, or 4.6 per cent. In 30 cases the hemolysis seemed to produce no result. No idea could be obtained in the literature of these cases as to what part the isoagglutinin played in the unsatisfactory result. The agglutination certainly could not have been observed without a microscopic examination.

¹² Zentralblatt f. Gynäkologie, 1920, No. 41.

With the view to study the question further the writer made a series of investigations from a certain number of persons. About 10 cc of blood was taken and an abundant supply of serum thus obtained. One or 2 cc of blood and 1 per cent physiological salt solution were placed in vessels to separate the plasma from the red blood cells; by the use of a centrifuge the blood corpuscles were separated from the plasma. This was done under careful aseptic precautions, so that bacteria were excluded. Various dilutions were then studied, but it was found that the behavior of the plasma was practically the same in various degrees of dilutions. Portions of this serum of various blood solutions were then added to the fluid from which corpuscles had been removed, and these various series were studied. It was observed that red blood cells from one person would agglutinate perhaps with the serum from two different persons, and when pregnant patients were studied the results were also noted. Thirty-eight persons were used in the study in five series and 236 comparisons of serum and blood corpuscle mixtures were made. In these 236 comparisons there were 10 positive instances of hemolysis and 94 examples of agglutination. If in practice the blood of two persons instead of one were examined at the same time it was found that a more accurate result could be obtained. By this method of systematic examination isoagglutinin and hemolysis can be demonstrated without great difficulty. Unless there is haste in a given case of transfusion every effort should be made to thoroughly test the blood of the donor and the recipient. When there is a profuse hemorrhage requiring prompt action a test may be made, using only 20 to 30 cc.

Appendicitis in Pregnancy. Hoffmann¹³ reviews the literature of the subject, which calls attention to the varying position in which the appendix is found in pregnant and non-pregnant patients. Reproductions of *x-ray* pictures are shown, indicating that the appendix normally hangs over the pelvic brim and is to be found just at the border of the pelvis. The writer studied the position of the appendix in pregnant patients by giving barium, and four hours afterward taking an *x-ray* picture of the cecum. The pregnant patient is placed upon the abdomen as far as possible, and also upon the abdomen and the back, especially if the patient had relaxed abdominal muscles. The best pictures were obtained with the patient lying upon the abdomen. These *x-ray* pictures indicated the head and vertebral column of the fetus and showed how much the appendix was drawn up in the pregnant condition. It is found at the crest of the ilium in practically all of the cases. In some the tip of the appendix projected over upon the ilium and in a few extended down along the concave anterior surface of the pelvic brim. Thirty-one patients were so examined and the appendix was found in a few instances a finger-breadth above the crest of the ilium: in most of the cases a finger-breadth below the crest of the ilium.

He adds to these cases studied by the *x-ray* 8 cases of pregnant women having appendicitis who came to operation, and his paper contains two illustrations, one a reproduction of a photograph and one an *x-ray*

¹³ Archives f. Gynäkologie, 1920, No. 112, p. 230.

picture taken from these patients. In 1 case the appendix and the head of the cecum were pushed up to the border of the ribs by the uterus at full term; underneath the appendix was the right Fallopian tube adherent to the peritoneum of the abdominal wall, and the right round ligament and spermatic vessels were in practically the same location. This patient died undelivered from a sudden and profuse hemorrhage into the brain, and therefore a dissection of the appendix could be made without difficulty. It showed that she had a chronic appendicitis with adhesions as described.

The second patient was brought in moribund, in eclampsia, dying undelivered, and autopsy showed the appendix empty of feces and drawn up into practically the same position. Another patient had appendicitis during a previous pregnancy and declined operation. She afterward came in at term with acute appendicitis and was operated upon, and the appendix was found retrocecal and very deep in the abdomen and pelvis. This patient recovered from the appendicitis and gave birth spontaneously to a living child. Another patient, brought in at the eighth month of her tenth pregnancy, died in the ambulance, having chronic nephritis and degeneration of the heart. The tissues were very much relaxed and there was marked prolapsus of the abdominal viscera. Here the appendix was not drawn upward. Another patient was delivered by Cesarean section, having been brought in suffering from acute appendicitis with purulent peritonitis. The appendix was not drawn up in this case, but was at the right sacro-iliac joint and fixed by old adhesions. Autopsy showed streptococcus infection to be the cause of death.

In two cases in which the uterus was extirpated to end pregnancy complicated by tuberculosis the appendix was at the brim of the pelvis and at the right sacro-iliac articulation. Another patient, seven months pregnant, had pain and tenderness in the abdomen and the appendix was found retrocecal.

In studying these cases a definite relation between the degree of tensesness of the abdominal wall, the size of the uterus and dislocation of the cecum cannot be established. In primiparous patients with tense abdominal walls at the end of pregnancy it is not rare to find the appendix pushed upward, while in multiparous patients with fairly strong abdominal walls at the seventh month of pregnancy the appendix is pushed up to the crest of the ilium. It was recognized that the diagnosis of appendicitis in pregnancy may be difficult because of symptoms simulating other conditions.

If the barium and x-ray method are used valuable information may be gained, but this cannot be done in an acute case, and would only be useful for interval operation to determine the most favorable location for incision. The majority of obstetricians believe that pregnant patients showing symptoms of appendicitis should be operated upon as soon as there is good reason to believe that appendicitis has developed, and in these cases examination by the x-ray would not be practicable.

The reviewer has had occasion repeatedly to operate upon pregnant patients suffering from appendicitis. He can recall only two cases in

which the appendix was in the same position. It is his belief in operating upon women for conditions of pelvic or abdominal inflammation that the incision should always be made in the median line, and that when the abdomen is opened the operator may complete his diagnosis and prolong his incision as may be necessary to deal satisfactorily with the condition present. In the reviewer's experience the appendix is found usually in pregnant women in one of three locations: (1) adherent to the broad ligament or uterus near the pelvic brim; (2) retrocecal; (3) as high as the ilium and often retrocecal at that point.

In cases of old appendicitis complicating pregnancy, on opening the abdomen an encysted collection of pus and gangrenous material may be found. If such be the case every effort should be made to drain this through the abdominal wall at the nearest point by passing a soft-rubber tube through the wound in the abdominal wall at the elected point; but it is questionable whether it is possible to accurately plan an incision in the abdomen of a pregnant woman suffering from appendicitis, which will surely bring the incision over the location of the appendix.

Artificial Perforation of the Uterus in the Early Months of Pregnancy. Petzold¹⁴ discusses the question of perforation of the uterus in the early months of gestation. He finds that the instrument most often at fault in 97 cases was the placental forceps or uterine dressing forceps in 53, in 18 the curette caused the wound, in 8 the Hagar dilator, in 6 a sound or bougie, in 1 a laminaria tent, and in 8 cases a catheter or pointed instrument.

Women who operate upon themselves are the most dangerous of all operators. By them the nozzle of a syringe or part of a pessary, a stilette, a knitting needle, a hair pin or a pencil, or any object which is practically rod-shaped may be employed. The most usual location of the perforation of the uterus is in the normal position in the posterior wall of the lower uterine segment; if the uterus is retroverted, the injury is in the anterior wall of the lower uterine segment; in rare cases, when the uterus is deflected to one side, the injury occurs just above the internal os on the side opposite from that to which the uterus is drawn. It is possible, however, for perforation to be in the fundus or at a point where the tubes enter the uterine wall. In 32 cases where this was made out clearly the posterior wall of the uterus was wounded in 16: in 8 the anterior and in 8 the fundus. In one case the bladder was separated from the cervix and the whole anterior wall of the cervix was lacerated. In accordance with the instrument used, and the skill or lack of skill of the operator the injury produced varies greatly. When the cervix is dilated with metal dilators the lacerations or wounds are in the mucous membrane and muscular tissue, especially at the internal os. If the operation has been done under aseptic precautions these wounds do not expose the patient to very great danger. The opening of the peritoneum and the wounding of the uterine and spermatic vessels are important complications. When the uterus is perforated with the

¹⁴ Archives f. Gynäkologie, 1920, No. 112, p. 291.

finger these complications do not exist. When severe wounds occur the intestines may be involved, and especially the small intestines and portions of the mesentery may be torn off; even the ureter has been injured and the folds of the broad ligament may be so damaged that section is necessary to control the injury inflicted.

The result of the wound will depend upon its location and extent of the injury, whether it was produced with violence or not and whether aseptic precautions were practised during the manipulation which caused the injury. When the peritoneum is opened and the intestines or bladder are injured the condition is evidently one of great danger. The writer reports 4 cases, of which 3 had developed during the last five years. Cases may be divided into those in which injury was produced by instruments where the wound has been inflicted by a physician or where injury was done by the patient with criminal intent.

Petzold's first case was that of a patient who had a pregnant retroflexed uterus which had become incarcerated at the end of the second month; she had also inflammation of the left tube and ovary. Profuse hemorrhage followed her admission, which indicated that abortion was inevitable and that the uterus should be emptied. The introduction of a sound showed the uterus 12 cm. long, and the hand placed upon the abdominal wall could feel the end of the sound. The uterus had been perforated in the anterior wall. Section was immediately performed and the wound readily detected on the anterior surface of the uterus. On the left side there was a large tuboövarian abscess which was attached to the posterior portion of the broad ligament; this when emptied was found to contain thin, inodorous pus having abundant leukocytes, but no bacteria. To avoid danger of infection to the peritoneal cavity the uterus was completely removed. Microscopic examination showed that the end of the uterine sound had carried elements from the lining membrane of the uterus and decidua up to the abdominal peritoneum.

The second case was that of a patient who had been curetted by a physician for abortion; the uterus was perforated by placental forceps, the intestines prolapsed down to the vulva, but were immediately replaced, the vagina was tamponed and the patient was brought into the hospital. On admission there was slight bleeding from the vagina, profound anemia, small, irregular pulse and the abdomen was distended and very sensitive. Intravenous saline transfusion was practised; the abdomen was opened and was found to contain a large quantity of red fluid blood. On the anterior aspect of the uterus there was a wound in the uterine wall, about as large as a cherry, from which blood was flowing. When the intestines were examined no wound could be found; when the point of perforation was carefully cleansed with gauze, placental tissue could be seen protruding through the rent. The uterus was amputated through the lower segment, but the patient died ten minutes after the operation. At autopsy there was profound anemia, moderate distention of the large intestines, while the small intestines were collapsed; near the ileocecal valve there was a rent in the mesentery; whether large vessels at that point had been opened could not well be determined, nor could anything further be made out except the extensive

wound of the mesentery. A portion of the intestines, eighteen inches long, had been separated from its mesentery. The serous covering of the intestines in two places was torn and bleeding, and in one of these the intestines had been wounded; but it could not be made out that the wound had penetrated into the lumen of the bowel. The greater portion of the placenta was still in the uterus, although part of it had been forced through the wound.

His third case was that of a woman who had had children and had her last period about four weeks before admission. She had then introduced the nozzle of a syringe into the uterus, causing sharp hemorrhage. A physician was called who inserted a laminaria tent, and told the patient to remain quiet in bed, believing that the embryo would be spontaneously expelled. A solid dilator was afterward introduced and later the physician inserted placental forceps and drew out a portion of the intestines. The patient was immediately brought into the clinic. On admission she was considerably shocked and there was vaginal hemorrhage. There also was a tendency to vomit and to pass gas from the bowel. The abdomen was not distended or sensitive. On opening the abdomen there was a small quantity of blood at the bottom of the abdominal cavity. The uterus had been perforated on the posterior wall two finger-breadths beneath the fundus; the edges were not smooth and the peritoneum had separated itself from the muscular tissue and was open in a number of places. The uterus was amputated through the lower segment and the ovaries allowed to remain. When the abdominal condition was examined a loop of the ileum had been injured, loosened from its mesentery and torn for about 10 cm. in length. This portion of the bowel was removed and joined to the uninjured portion, care being taken to keep the tissues dry during the operation. The patient received saline transfusion and stimulants. She developed an acute purulent peritonitis with intestinal disturbance, and died on the twelfth day after operation. Autopsy revealed the peritonitis and the fact that at the point of resection the intestines had healed soundly and smoothly. Above this point, about 10 cm., there was a perforation of the bowel about 6 mm. long. The uterus was the size of a fist and considerably lacerated in the region of the external os, torn upon the left side and infiltrated with blood. On the anterior portion of the uterus there was an area where evidently the placenta had been attached, and the cervical canal was somewhat dilated. The fundus of the uterus was tightly contracted, so that the whole organ assumed an hour-glass form. Just above the internal os there was the head of a very young fetus. On the border between the decidua vera and attachment of the ovum there were obliquely extending lacerations through the anterior uterine wall.

His fourth case was that of a multipara who had had two normal labors and one abortion. She stated that she was pregnant and that she had taken an injection of tepid water; shortly after this hemorrhage occurred. A physician had been called who had applied a tampon. On the following day she stated that the tampon had been spontaneously expelled and that profuse hemorrhage and fever shortly afterward

developed. As the patient was suffering from profuse hemorrhage on admission she was at once operated upon. A fetus and a mass of fluid blood were found in the vagina. On the anterior lip of the cervix there was a wound about the size of a quarter-dollar and on the left of this there was an opening extending up toward the termination of the cervix. After the uterus had been completely emptied no further injury could be found. Evidently the wound and the fistulous tract had been produced by the nozzle of the syringe. The patient recovered after the uterus had been completely emptied.

As regards cases in which lacerations occur through the use of instruments the lesions most commonly seen are opening of the vessels of the mesentery or some injury to the intestinal tract or an infection starting from the lower surfaces in the uterus. The plan of operation adopted for the relief of such a condition will depend upon the condition present.

Many operators in cases in which a sterile sound, catheter or solid dilator has made the laceration or wound believe that conservative treatment is indicated. In 15 cases in which the conservative plan was followed 13 recovered and 2 died of purulent peritonitis. If, however, the perforation has been made by the curette or by placental forceps conservative treatment is impossible and one must operate through the abdominal wall or through the vagina. Some would advise suture of the wound in the uterus through the vagina, and this might be accomplished by splitting the anterior cervical wall, removing the placenta under direct vision and then closing the perforation and uterine wound.

The majority of operators, however, believe that the abdomen should be opened in these cases, especially when one is not sure that more than a small perforation has occurred. The sooner the operation is done after the injury has been received the better for the patient, for if infection has occurred it will speedily develop and spread. Bleeding vessels are often found in the broad ligament, the mesentery or the mesocolon, and these naturally require ligation promptly. It has been stated that of those patients operated upon within a few hours of the injury two-thirds should recover, while those operated on as late as twenty-four hours after injury would show a recovery rate of only one-third. The use of sacro-anesthesia is considered valuable in these cases. When the abdomen is opened, while attention may first be given to the uterus the other abdominal and pelvic organs must also be thoroughly examined. The intestine should be gone over throughout its entire extent, and, as a rule, the uterus should be examined last of all, because a perforation in the uterus is less important than a wound in the intestines.

In 19 cases treated by closing the wound in the uterus by sutures and closing the abdominal cavity 18 recovered and 1 died from purulent peritonitis. In the majority of cases a small laceration is found in the uterus complicated by an injury to the intestines or the escape of placental tissue into the abdomen and the development of an infection. Some have drawn attention to the fact that in closing the wound in the uterus care must be taken not to include a portion of its lining membrane. When the uterus is opened in Cesarean section and afterward closed by suture, if a portion of its lining membrane is included in this

suture the danger of a rupture of the scar is increased. Others urge radical treatment by supravaginal amputation or total extirpation through the abdomen. The choice is largely one which the operator may make in accordance with his previous experience. Amputation has been considered the most prompt and efficient method, with less attendant danger than the extirpation of the uterus. Others believe that extirpation is best because a cleaner and better wound is left and because the danger of infection from the uterus is thus removed. If tincture of iodine is applied to the genital tract through the abdominal wound or through the vagina the danger of infection is clearly reduced. In 30 cases of instrumental perforation of the uterus treated by extirpation of the uterus 24 recovered and 6 died. Among those operated on by supravaginal amputation there were 4 recoveries and 1 death. When results are compared it is interesting to note 2 cases reported in the literature admitted to the hospital with general purulent peritonitis; they were treated by total extirpation, while 1 case having an extensive laceration of the uterus which extended into the parametria, and 1 case with perforation of the uterus and sigmoid flexure were treated by amputation. This series of 5 cases may be contrasted with others, but it seems difficult to draw a positive conclusion. When an attempt is made to close the uterine wound the edges should be brought together accurately and the peritoneum closed over the line of suture to prevent the spread of infection from the uterus into the abdominal cavity. When laceration of the uterus occurs in such a position that closure can be made safely this should be attempted. The age of the patient must be taken into consideration, and if she is comparatively young and capable of bearing children the uterus should not be sacrificed. When wound of the intestines is feared but cannot readily be found it is often useful to distend the bowel with some suitable and harmless gas.

In deciding upon extirpation of the uterus, positive evidence that severe infection has developed should lead to this method of operating.

In cases in which operation was postponed until twenty-four hours after original injury the total extirpation of the uterus is still the method of choice. If one delays in these cases any longer the only opportunity for cure may be lost.

The Calcium Content of the Blood in Pregnancy and Parturition and also in Nephritis and Eclampsia. Kehrer¹⁵ has made a series of investigations to determine the calcium content of the blood in parturient women. He finds that the quantity of calcium in the blood of healthy human beings varies to a slight degree only. Among healthy women from twenty to forty years of age the average was 10.18 mgm. calcium oxide in 100 cc of venous blood. This was thought to have possibly something to do with the lack in the development of the skeleton and the prevalence of rachitis among the people of Saxony.

When disease of the pelvic organs develops accompanied by free hemorrhage the percentage would fall as low as 9.26 mgm., and sometimes even lower than this. There seems to be some relation between

¹⁵ Archives f. Gynäkologie, 1920, No. 112, p. 487.

the quantity of blood and the formation in the body of the calcium salts, and the substance known as prothrombin may be of significance in cases after hemorrhage has developed.

In the first half of pregnancy there is practically no alteration in the calcium content of the blood: in the last six weeks of pregnancy the average was 9.22 and 9.25 mgm. calcium oxide. On the eighth or ninth day of the normal puerperal period, the patient nursing her child, the calcium content averaged 8.96 or 9.29 mgm. There was a close resemblance between the calcium content of the blood in the later portion of pregnancy and the early days of the puerperal period with the woman nursing her child, and calcium oxide was diminished in quantity at the end of pregnancy and the first days of the puerperal period; the body of the mother loses in calcium, but the mechanism of this loss is so regulated that it does not ordinarily produce disturbances. In labor while uterine contractions are going on there is a small loss of calcium from the blood. In cases of nephritis and eclampsia in pregnancy the calcium percentage reached as low as 8.17 or 7.67 mgm. of calcium oxide. When women in the puerperal period have nephritis and eclampsia, even though the patient be kept exclusively upon a milk diet, the percentage of calcium does not rise to normal. The writer states that his study of these conditions, including also his study of the contents of the blood in cases of diabetes and tetany both during and after pregnancy, and also in patients subjected to operation or castration by the x-ray, has not brought him to a point where he can make definite conclusions.

Premature Separation of the Normally Attached Placenta. Lieven¹⁶ contributes a paper in which he describes five cases and adds an illustration showing the body of the uterus.

His first case was that of a multipara whose pregnancy has been normal up to the ninth month, when she had severe pain in the abdomen, thirst, a chilly feeling and free movements of the bowels. Upon examination when admitted to the hospital the abdomen was distended, the uterus could be made out but did not seem to be especially tense. No fetal heart sounds could be heard and there was no hemorrhage. The patient was given morphine and ten hours later suddenly a very profuse hemorrhage occurred. The cervix would admit one finger, the membranes were unruptured and on examination one could not find a placenta. A firm tampon was applied, and this was followed by development of strong uterine contractions. It was difficult to make out the precise position and presentation of the child, and heart sounds could not be heard. After removing the tampon the cervix admitted two fingers, but placental tissue could not be found. Under anesthesia the membranes were ruptured and version was performed, with the bringing down of a foot. Pituitrin was given and in a half-hour the body of the child had been expelled up to the head, which was perforated. While the head was being delivered there came from the uterus a considerable quantity of dark blood followed by the placenta. Shortly after this a

¹⁶ Monatschrift f. Geburtshilfe, 1920, vi, No. 51, 377.

very severe hemorrhage occurred, accompanied by absolute atony of the uterus, and the death of the patient followed in about an hour.

At autopsy all of the organs were found in an intensely anemic condition, but without pathological lesions. On the anterior surface of the uterus there were many large and small longitudinal lacerations of its peritoneal covering, and some of these extended through the peritoneum and into the muscular tissue. On the inner surface of the uterus the point where the placenta had been attached could plainly be made out and the lower border of the placenta had been very close to the internal os. In the placenta itself there were lesions along the border which showed that the placenta had separated before labor began.

The second case was a primipara, aged twenty years, in the tenth month after a normal pregnancy. After using a sewing machine a profuse hemorrhage suddenly occurred and the uterus was distended and sensitive. The child could not be made out and the heart sounds could not be heard, and on internal examination the placenta could not be felt. A tampon was applied by the physician who first saw the patient, and she was brought to the hospital. As hemorrhage had ceased it was thought best to delay to enable her to rally somewhat. Eight hours later the temperature had begun to rise and the cervix was partly dilated. The child was dead and its head was perforated, followed in about forty minutes by spontaneous birth. The placenta was delivered ten minutes afterward, and with it a very considerable blood-clot. A considerable portion of an old blood-clot was spread over the placenta and adherent to it. There was also an extravasation of blood beneath the amnion in one portion.

In his next case a profuse hemorrhage occurred in a pregnant woman with no dilatation of the cervix. The child's heart sounds could be heard and the urine contained no albumin. Under sacral anesthesia Cesarean section was practised with transverse fundal incision, which fortunately escaped the placenta. A living child was delivered, and as soon as the child was delivered the greater portion of the placenta came up through the uterine incision. Supravaginal amputation of the uterus was practised and a large clot was found within the uterus. The mother and child made good recoveries.

A multipara, six hours after pain began, had sudden and profuse hemorrhage and pronounced tension in the abdomen. The cervix was partly dilated; the placental tissue could not be found. Shortly after admission to the hospital uterine contractions became efficient and a dead child covered with blood was born. When the placenta was delivered a large blood-clot accompanied it. On examination the placenta seemed to be divided into two halves, of which one was normal, and in the other half there were the remains of an old hemorrhage. There was a sharply defined line of separation between the two portions of the placenta and the smaller portion was only half the thickness of the remainder.

A multipara, as soon as labor pains began, had distention of the abdomen which made it impossible to accurately map out the fetus or hear fetal heart sounds. On internal examination there was partial

dilatation with unruptured membranes and the head partly movable. Shortly after the examination the patient collapsed. With hope of lessening the tenseness of the uterus the membranes were ruptured, when the amniotic liquid escaped, colored with dark blood. A living child was delivered by forceps, when, on examination, a second was found; the membranes were ruptured and this child was extracted by the feet. The placentaë were fully developed and united only by the membranes. In one of them there was a dark blood-clot and placental tissue itself infiltrated with blood. The other placenta showed nothing of pathological interest, but there had been a hemorrhage between the fetal membranes forming the collection of blood.

In the next few years 22 cases of premature placental separation were admitted to the hospital. In 4 of these the placenta was completely separated and in 7 partially. In 2 cases the umbilical cord was abnormally short, in one measuring but 26 cm. In the remaining 11 cases the mothers recovered from the accident: 5 of the children were born living and 6 died. In 2 cases the Porro operation was performed with good result; 4 of the others were treated by version and extraction. In 3 the membranes were ruptured and in 2 the use of pituglandol and morphine ended with labor. In 3 cases after the birth of the child there was copious postpartum hemorrhage, which was controlled in the usual method. In these 11 cases there was no albumin in the urine.

In the 16 cases in all there were 5 of complete separation of the placenta. In 1 patient the urine contained albumin and the others none. One mother died from uterine atony; 3 others had severe postpartum hemorrhage, from which they recovered. In 7 of the cases the child was born living, the remainder were dead or died during birth, a mortality of 56 per cent. One of these was a twin pregnancy, and as soon as the membrane of the first child ruptured the placenta of the second became partly separated. These cases occurred among 6955 births and would give some idea of the relative frequency.

The writer ascribes this accident to pathological conditions in the uterine decidua. The question naturally arises, What causes these decidual changes. Toxemia is the agent usually blamed for this accident. Among these patients but one of them had albumin in the urine, and hence nephritis could not be ascribed as the cause of the changes in the uterine decidua. When attention is drawn to the condition of the uterine muscle and specimens were examined microscopically there were no gross changes. There was no evidence of inflammation, but the lesions were those essentially of the chronic metritis and a disturbance of the normal relationship of the muscular fibers of the connective tissue. Connective tissue seems to have increased at the expense of the muscular fibers, which were very considerably shortened. Such changes in the muscles would produce atony, and this would be an important factor in placental separation. In such a case shortness of the umbilical cord and resulting pull on the placenta might readily cause it to separate.

In the treatment of these cases indication is clear to empty the uterus as soon as possible. Cesarean operation is the most prompt and efficient method, and this may be accompanied by extirpation of the

uterus or amputation, as the condition of the patient may suggest. The mortality for children is 60 per cent. In appreciating this an operator must throw no chance against the mother for the sake of the child.

Heidenheim¹⁷ reports a case in a multipara suddenly taken with severe abdominal pains. She was sent to the hospital with a provisional diagnosis of internal hemorrhage. On examination the urine contained albumin and granular casts. The patient was exceedingly pale, with some edema of the legs and the uterus exceedingly painful. It seemed to be greatly distended; fetal movements could not be felt nor could heart sounds be heard. There was no dilatation of the cervix. As soon as narcosis was begun by ether the uterus very markedly enlarged, and this was positive evidence that internal hemorrhage was going on. On turning the uterus out of the abdomen the wall was found infiltrated with blood; there was hemorrhage beneath the serous covering of the uterus. The uterus was amputated without opening it and the membranes were not ruptured during the operation. The cervix was closed with interrupted sutures and the peritoneum brought over the wound. The abdomen was closed without drainage. Intravenous transfusion was given as the operation terminated. The patient made a good recovery although the hemoglobin was but 30 per cent after the operation. Arsenic seemed to be the therapeutic agent which helped most in her recovery.

On examining the placenta there was no anatomical evidence that nephritis had caused the lesion which led to its separation; there was a large clot behind the placenta. After the operation the albumin disappeared speedily from the urine. It is interesting also to note that the umbilical cord was but 39 cm. long and was coiled around the neck of the child.

Indications for Interruption of Pregnancy. Von Jaschke¹⁸ discusses the question of what constitutes proper indications for the interruption of pregnancy. He recognizes the fact that this problem is complex, and that not only medical, but sometimes factors in economics and sociology may enter into the discussion. A complaint of a patient in the pregnant condition suffering from some of the minor ills, that pregnancy must be terminated because she is ill, must not be taken seriously. Experience shows that if pregnancy is interrupted in these patients the infection from which they suffer is made much worse. Pelvic contraction of considerable degree is also not an indication for the interruption of pregnancy. In tuberculosis and diseases of the heart the situation is different.

A table is given of the diseases complicating pregnancy and the number of cases of each in which interruption of pregnancy was accepted and denied. The total number of cases was 663. In tuberculous women pregnancy was interrupted in 67 and refused in 26. In diseases of the heart pregnancy was interrupted in 17 and refused in 9. In pronounced anemia pregnancy was interrupted in 27 and refused in 25. In disease of

¹⁷ *Monatschrift f. Geburtshülfe*, 1920, iii, No. 51, 145.

¹⁸ *Ibid.*, iv, No. 51, 232.

the kidneys pregnancy was interrupted in 7 and allowed to go on in 6. In the pyelitis of pregnancy, in 32 cases pregnancy was stopped and in 31 allowed to go on. In diseases of the mind and nervous system, in 12 cases pregnancy was interrupted and in 8 it was not. In cases in which pregnancy seemed an unendurable proposition in proportion to the strength of the patient pregnancy was ended in 10 and allowed to continue in 10. In varicose bloodvessels therapeutic abortion was performed in 2 and refused in 2. Pregnancy was terminated 149 times because of hemorrhage, excluding dangerous placenta præviæ, and in 109 patients pregnancy was allowed to continue. In contracted pelvis pregnancy was interrupted but twice and allowed to continue in 1. A similar experience was obtained in osteomalacia. In Basedow's disease pregnancy was interrupted in 2 cases and refused in 2. Eleven cases of pregnant women having tumors had pregnancy interrupted and 10 had not. An equal number of patients had pregnancy interrupted and refused in obstinate constipation, diastasis of the rectal muscles, exudate in the pelvis, inflammation about the sigmoid flexure, infection of the Bartholin glands, retroflexion of the uterus, gall-stones, osteomalacia and prolapse of the uterus. Pregnancy was interrupted once in abscess of the lung and once in intestinal obstruction.

Stress is laid upon the point that one cannot judge a given case by a class of cases but by the circumstances of each individual patient. In tuberculous women the opinion has been gaining ground that if pregnancy is interrupted it should be accompanied by sterilization, and this principle should be extended to all diseases complicating pregnancy which threaten to become chronic and which would jeopardize the life of the mother at each recurring pregnancy. Such would be true not only of tuberculous women but those suffering from chronic disease of the heart and kidneys.

One must recognize cases in which, from the standpoint of eugenics, it is undesirable that the woman continue to produce children. If valid excuse arises for interruption of pregnancy sterilization may be added. When tuberculosis is not pulmonary it is often necessary to interrupt the pregnancy and afterward give the patient appropriate treatment for the existing tuberculous condition. Where one kidney is tuberculous this can often be extirpated without interrupting the pregnancy. In dealing with disease of the heart, spinal anesthesia is advised, and wherever possible operation through the vagina or lower uterine segment. It is recognized that in heart cases in which compensation is good and the general condition favorable, pregnancy should not be interrupted unless signs of failing compensation appear. Rest in bed and the use of digitalis will often improve these patients and enable them to go on to the end of gestation. When interruption is practised in the later months of pregnancy, Cesarean section with spinal anesthesia is the method of choice. In women who have borne a number of children, sterilization should be practised. It is often difficult to make a distinction in cases of pregnancy complicated by chronic disease of the heart muscle. If the patient has suffered from lack of compensation before the beginning of pregnancy, then pregnancy may be unendurable and interruption

should be accompanied by sterilization. In primiparous patients sterilization may be postponed until the patient has had an opportunity to obtain more than one child. In chronic disease of the bloodvessels each case must be studied upon its own merits, and in the majority pregnancy need not be interrupted. The writer repeats his warning that acute infection complicating pregnancy never calls for interruption of the pregnancy. The infection should receive attention and the general strength of the patient be maintained. If abortion or labor develops it may or may not injure the chances of the patient for recovery.

Pernicious anemia is comparatively rare in pregnancy. Should this develop and prove threatening, pregnancy must be interrupted by that method which will be followed by the least loss of blood and permit blood transfusion during the interruption or soon after. Death often occurs in these cases during or immediately after labor, and this danger should be anticipated. Evidently in hemophilia pregnancy should not be interrupted and in leukemia only for positive indications.

Disease of the respiratory apparatus, excepting tuberculosis, does not require the interruption of pregnancy, and the same is true of appendicitis, which should be dealt with by operation. In dealing with disease of the kidneys, casts or albuminuria, retinitis is always a sign of great danger and usually calls for prompt interruption of pregnancy. If nephritis is chronic, sterilization should be practised. In constitutional disease accompanied by disorder of the internal secretions it is often necessary to interrupt the pregnancy. It is estimated that in Basedow's disease 60 per cent of the patients are made much worse by pregnancy and in 20 per cent the original diseases become so bad as to demand interference; 4.6 per cent died during pregnancy or soon after labor from acute failure of the heart; evidently this condition is a very serious one and should be closely watched, and interference be practised promptly before the condition becomes critical. In cases of struma, operation may sometimes be possible without the interruption of pregnancy. When there is persistence of the thymus gland cases are unusually dangerous. In multiparous and critical cases sterilization should be practised. When struma alone complicates pregnancy it is well not to interrupt gestation, but operate upon the goiter, and a mortality as low as 2 per cent has been obtained in these cases with only 6.5 per cent interruption of pregnancy following the operation.

The writer saw two patients pass through gestation successfully where the goiter was so large that the trachea was compressed in the typical saber form. In three-fourths of cases of osteomalacia medication stopped the process and permitted pregnancy to go on; in one-fourth interruption accompanied by castration should be performed, but care should be taken to limit this operation, if possible, to multiparæ and women who are not young. In the tetany of pregnancy, medical treatment should first be tried before interruption is practised. Ninety-five per cent of diabetic women are sterile, but if conception occurs, pregnancy may exercise an unfavorable influence on the original disease. The mortality after labor is estimated as high as 20 per cent, and death often occurs in coma. Before interrupting pregnancy the effect of diet and thorough

medical treatment to control acidosis should be tried. In interrupting pregnancy, special care must be exercised to secure strict asepsis, as infection readily develops. Methods of gradual dilatation of the uterus should be declined, as vaginal hysterectomy is the operation of choice.

In the pronounced nausea of pregnancy one must not interrupt too early, as much can be done by thorough medical treatment. Care should be taken to recognize serious symptoms and not allow the patient to go to the point of threatened coma, which will usually end fatally. The ptyalism and cutaneous complications of pregnancy do not call for interruption. When acute yellow atrophy of the liver is threatened, pregnancy must end at once; to continue is often so serious that death speedily occurs in spite of treatment. In disease of the mind, brain and spinal cord some condition must be present which threatens life to justify the interruption of pregnancy. In myelitis or multiple sclerosis it may be best to interrupt the pregnancy, for these diseases are often greatly enhanced by gestation. In the psychoses the pregnancy should usually be allowed to continue; such is the case of patients who threaten suicide. If chorea develops and is apparently the result of infection a mortality of 20 per cent in these cases is not unusual. Heart complications are often present, and it may be necessary to interrupt the pregnancy promptly. Epilepsy, hysteria and neurasthenia very rarely call for the interruption of gestation. In general the interruption of pregnancy should not be hastily done and efforts should be made to control threatening conditions.

In the *treatment of accidental hemorrhage*, some would rely upon morphine, and if the hemorrhage did not cease, Cesarean section. Placenta previa, it was thought, yielded better to direct pressure. In multiparæ, version and the use of the breech as a plug were thought of value, and in primipara with closed cervix and increasing hemorrhage, Cesarean section. Others preferred to rupture the membranes and apply a tight binder and give ergot and pituitrin. Version for placenta previa will serve in many cases.

At St. Bartholomew's Hospital in 2600 patients, 98 had antepartum hemorrhage, 50 had accidental hemorrhage and 48 had placenta previa. The maternal mortality of the whole series was 6 per cent. and the fetal mortality 46 per cent; 37.7 per cent of these cases were delivered without interference; in others rupture of the membranes, version, dilatation and forceps, Barnes's bag, Cesarean section, plugging the vagina and the application of abdominal binder were all employed.

Spontaneous Recovery of an Early Tubal Gestation is reported by Schiffmann.¹⁹ His patient was aged thirty-two years, no previous labor or abortion. Amenorrhea of about three months with a history of one considerable hemorrhage for three weeks. Pain in the right lower abdomen. Examination under an anesthetic showed a suspicious thickening of the right lower abdomen which could not be made out. The patient left the hospital to return when bleeding or pain developed. Pain and fever brought her again to the hospital with a discharge of

¹⁹ Archives f. Gynäkologie, 1920, i, 133, No. 113.

bloody mucus, with a foul-smelling, watery fluid from the vagina. Indefinite symptoms continued and the patient was operated upon. The intestines showed flecks of fibrin with inflammatory adhesions over the pelvis. On loosening these and ligating some, a tumor as large as a fist was found at the right cornu of the uterus; this contained a placenta and fetus between three and four months, which had escaped through the rupture of the tube. There was no blood in the abdomen or vicinity of the uterus, but pus was present also in the pelvis. The intestines were distended and they were punctured and emptied, closed by stitches, drainage inserted and the abdomen closed. In the pus were found streptococci in pure culture. The patient died of purulent peritonitis following rupture of an interstitial pregnancy. There was also lobular pneumonia and fatty degeneration of the heart, liver and kidneys. There was no thrombosis.

A microscopic study of the specimen was made which showed that an old inflammatory process had existed in the tube, followed by acute purulent infection with streptococci. There had been an active inflammation of the sac of the embryo with formation of pus at various portions and the presence of streptococci. The examination of the uterus showed the presence of streptococci without development of decidua or uterine glands. A minute study was then made of the anatomy of the various portions of the genital canal and of the specimen. The pregnancy had been interstitial; there had been a salpingitis preceding the rupture of the tube which had not caused hemorrhage by peritonitis.

He adds the case of a primipara kept in the hospital under observation for three days, with a diagnosis of tubal pregnancy on the left side. Abdominal section showed the correctness of the diagnosis and the left tube and ovary were removed. In the middle third of the right tube there was also a swelling, and this tube was removed, leaving the ovary. The patient made a good recovery. On opening the tube it was found to contain a blighted ovum or mole; absorption and organization of the tissue was going on, representing the spontaneous disappearance of the ectopic ovum and proving that in many cases of ectopic gestation such must occur. The paper is interesting for its microscopic study and histological illustrations.

Complement Deviation in the Diagnosis of Pregnancy. Fieux and Mauriac,²⁰ described 151 cases at the Brussels Congress in which the effort had been made to diagnosticate pregnancy by studying complement deviation. In the first series, antigen obtained from villi of the chorion was used and added to the serum of pregnant women at about one to four months, and this same experiment was repeated with the serum of women who had just been delivered prematurely of the product of conception. In 31 out of 34 of these cases, complement deviation was obtained.

On the contrary with the serum of women not pregnant or with those more than five months advanced, or in the case of women in whom there

²⁰ *La Gynécologie*, February, 1920.

was still present in the uterus a dead embryo, either entire or in part, there was no complement deviation.

In experiments under well-defined conditions, complement deviation should be taken as of diagnostic value. The objection to the method lies in the fact that it is difficult to carry it out accurately and that the reaction is a very delicate one and hence could easily go astray.

In the discussion of this paper it was brought out that one observer had obtained a positive reaction from two to ten months of gestation. The same investigator had found the deviation absent in fifteen healthy women. Unfortunately for the diagnostic value of the method, it gave positive results in malignant growth, fibroids and pelvic infections.

A New Reaction in Pregnancy and its Theoretical Explanation. Linzenmaier,²¹ draws attention to a condition of blood in pregnant patients in which the red blood corpuscles sink much more rapidly than do corpuscles in women not pregnant. If such blood be taken and maintained in a fluid condition the blood corpuscles remain so sharply defined and collect and sink so completely that it is possible to measure the blood sediment. This, furthermore, happens only in the blood of pregnant patients. Attention was first called to this phenomenon by a Swedish observer, Fåhræus.

Linzenmaier has endeavored to make the same observation in a more extended scale. He used a number of glass vessels, each containing more than 1 cc and having a breadth of 5 mm. These glass vessels were variously marked, the upper mark showing a counting of 1 cc, and a scale was marked upon the vessels showing 6 mm., 12 mm. and 18 mm.

To maintain the blood in a fluid condition, 5 per cent solution of citrate of sodium was employed, and in withdrawing the blood a syringe holding 1 cc was employed, and at each puncture 0.2 cc was used. After withdrawing the blood a note was made as soon as the corpuscles had settled to a certain point. The method was tried in over 300 cases. When normal patients were examined it was found that five or six hours was required for the blood to settle and for the plasma to reach the mark 18 mm. There were, of course, individual variations, but this remained about the average. In one case ten hours were necessary for the sediment to form, which was practically the same time required for blood taken from male patients. When menstruation was present in the non-pregnant, but three hours was required for the phenomenon. When repeated examinations were made on the same patient at various periods during menstruation, it was found that the time varied one or two hours.

One hundred pregnant patients in the hospital, whose periods ranged from seven to ten months, showed that with one exception the blood deposited a sediment in less than two hours. In patients pregnant four, five and six months never over two hours. The only exception to this was that of a woman pregnant seven months, who, unfortunately, was discharged from the hospital before a second observation could be made.

²¹ Zentralblatt f. Gynäkologie, 1920, No. 30, p. 816.

A period of two hours is taken as the probable average time necessary for the deposit of the blood in pregnancy. As pregnancy advanced this period became considerably less, until in the last quarter of pregnancy it was on the average about fifty minutes. It seemed evident from these experiments that from four months' pregnancy on, the blood settled much more rapidly than in a non-pregnant condition. An effort was next made to determine whether this is present in pregnancy only and whether this behavior of the blood corpuscles is in any way dependent upon pregnancy.

Unfortunately it was found that women who had been exposed to cold, who had what is termed a "cold in the head," showed some evidence of this phenomenon. Patients who had high fever, with inflammation characterized by the form of exudate, exhibited the phenomenon in pronounced majority. This was especially true of those having tumors of the pelvic organs, parametritis and peritonitis. In these cases the blood corpuscles were deposited in from eight to ten hours, which far exceeded anything observed among pregnant women. The impression given was that the blood corpuscles sank, it is said, like a stone thrown into the water.

In the first three months of pregnancy from 10 to 40 per cent of patients did not show this occurrence. Evidently in ectopic gestation this would not be of use in diagnosis, because one could not distinguish between ectopic gestation and inflammation of the tubes or ovaries.

It is possible that this method may be of value in diagnosing pregnant cases earlier than the fourth month. During labor the formation of sediment occurred more rapidly than during pregnancy, and this persisted until eight or nine days after the birth of the child, when it began slowly to decline and at the end of three weeks reached the average for the non-pregnant.

In cases of malignant disease the time required for the deposit of blood sediment is abnormal.

Fähræus believed that the cause of this phenomenon was agglutination of the red blood corpuscles. Under the microscope it can be seen that when blood sediments quickly, the red cells take the position of rolls of coins. To explain this phenomenon investigations were made in a physiological laboratory, where it was observed that the blood behaved as do colloid substances in certain chemical reactions. It has long been observed that blood corpuscles, so far as electric reactions go, are negative. Any circumstance which increases this characteristic would increase the tendency to agglutination. Evidently, the manipulation which the blood received in these experiments had caused a positive reaction to develop, and this has been noted when blood has been treated in other experiments by other chemical substances.

An effort was made to study the chemical nature of agglutinin regarding its behavior to heat. Blood was subjected for one-half hour to a temperature of $56^{\circ}\text{C}.$, when it was observed that the corpuscles formed a sediment less rapidly. This result must have been produced by the counteraction of albuminoid bodies which developed during the experiment. A comparison was then made between citrated blood and defi-

brinated blood, when it was found that the defibrinated blood produced sediment very much more slowly than the other.

From his investigations the writer believes that fibrinogen tends to greatly hasten the formation of sediment in blood, and that this may be the substance which produces the phenomenon. When fibrinogen is formed, agglutinin seems to disappear partially by absorption. Various substances added to blood produce the same result, such as gelatin and gum arabic. These investigations point to conditions of interest regarding the behavior of blood corpuscles in various conditions prevailing in women. So far as the diagnosis of pregnancy is concerned, it is evident that the phenomenon can give no certain information.

Two Cases of Severe Illness Following the Extravasation of Blood into the Abdominal Cavity Complicating Pregnancy. Schweitzer²² reports the case of a woman, aged twenty-seven years, in the tenth month of her first pregnancy, who sustained an injury by a fall. Violent pain in the abdomen, accompanied by vomiting, developed. The pain became severe and the fever which accompanied it was sufficient to bring the patient to the hospital. On admission, she looked very ill and suffered greatly from shortness of breath. The abdomen was distended and everywhere sensitive. The pulse was small, 158; the temperature about 102°. There was no external bleeding. The uterus was distended, and after rupture of the membranes about two quarts of amniotic liquid escaped, and nine hours later spontaneous labor occurred. After the emptying of the uterus, typical symptoms of severe peritonitis developed. On the left side of the abdomen there was dulness on percussion, vomiting increased and the temperature, which had fallen, became higher. On opening the abdomen, offensive gas escaped and a quantity of offensive pus, mixed with clotted blood. When this had been removed the cords of intestines could not be seen, as a fibrinous membrane completely covered them. The uterus was in the pelvis and the pelvic peritoneum was adherent to it. Drains were introduced and the abdomen closed. This extravasation of blood had become encephalated and infected, but, fortunately, this infection had been limited and had not become general. It was impossible to determine the precise point of origin of the blood. This might have been a rupture in the substance of the liver or a subserous rupture of the uterus or the bursting of a varicose vein in the left Fallopian tube or in the left broad ligament. The fact that dulness was most pronounced on the left side would indicate this. The pus contained streptococci, staphylococci and diplococci, and the source of infection was probably the intestine. As the patient recovered there was no opportunity to make a thorough autopsy and so the original lesion remained undiscovered.

The second case reported was that of a married woman, aged forty-one years, who had worn a ring pessary for a retroflexion and had had done a curetting, after which the patient was taken with severe pain in the abdomen, constipation, vomiting and distress. The physician made a diagnosis of ileus and the patient was brought into the hospital.

²² Zentralblatt f. Gynäkologie, 1920, No. 30.

On admission, her fever was not high, but her general condition was very bad. She was partly delirious and could not respond clearly to questions. The abdomen was distended and there was severe pain in the lower abdomen. A tumor could be made out which extended from the pelvis to the umbilicus. The vaginal portion of the cervix was drawn up very strongly and the posterior cul-de-sac was resistant and distended. The temperature was above 104° , and on abdominal section a considerable quantity of very offensive fluid, containing clots, escaped from the abdomen. There was evidently an extravasation of blood which had become infected. Apparently the patient had had a tubal pregnancy which had ruptured and the retained blood had become infected, or, in doing the curetting, the physician had perforated the retroflexed uterus and hematoma had formed and become infected. This patient grew better after the operation, and both patients ultimately made good recoveries.

Pregnancy and the Internal Secretions. Wintz²³ contributes a paper upon the effects produced by the substance taken from the Graafian follicle. The material for his researches was obtained by utilizing the ovaries of cows and swine, and for his first experiment a simple extract was made. This was done either by boiling or by the use of alcohol or by pressure. That substance which was obtained by pressure only was discarded as not pure and containing other products. In studying the product of the corpus luteum one must not forget the lipoids obtained from this substance and also the lipamins. These substances can be isolated and chemically distinguished. Lipamins stimulate menstruation, lipoid or luteo-lipoid checks it. These extracts were tested upon animals and also upon the human subject by giving them by injection. Observations were made upon blood-pressure, the coagulation time of the blood and other phenomenon. Some difficulty was experienced in testing the effect of these substances upon menstruation, but there was sufficient evidence that a definite effect was produced.

The injection of fresh corpus luteum substance in animals was followed by a brief fall in blood-pressure, succeeded by a return to the normal. The coagulation of blood was somewhat retarded by these substances. There seemed to be very slight action upon the genital organs of animals. In human beings the fresh luteal substance seemed to be inert.

Specimens of this substance which had been removed from the body for some time, and had been kept cold and sterile, were used. Such substances caused a rise in blood-pressure, with shortening of the coagulation time. The peristalsis of the bowel and genital tract was increased. Extract of corpus luteum produced by boiling caused a marked fall in blood-pressure, lengthening the coagulation time by shock, with abundant secretion of saliva, and, if used for some time, by loss of weight. There was much increase in peristalsis and swelling of the genital mucous membrane. A dark, bluish color developed in the genital tract, and in two cases in which menstruation had ceased this function returned.

²³ Archives f. Gynäkologie, 1920, vol. iii, No. 53.

It seemed to have little effect in checking excessive menstruation. With luteo-lipoid, coagulation time was hastened; there was no general effect, but menstruation was shortened and lessened, except in the case of patients having fibroid tumors, where the bleeding was increased. When lipamin was given, coagulation time was lengthened and there was discoloration of the mucous membrane, increase in menstruation and in discharge of blood. Placental extracts produced by boiling increased greatly the secretion of saliva and peristalsis of the intestine, and also respiration. A similar effect was produced by extract of cow's ovary obtained by boiling. It is interesting to note that luteo-lipoid and lipamin have opposite effects upon human beings.

Mahnert studied the effect produced upon pregnancy by disordered action of the endocrine glands. He finds that in 60 per cent of pregnant women examined there is deficiency in the function of the hypostasis. The suprarenals are disturbed in 40 per cent of the patients while the ovaries and the suprarenals are both deficient in action in from 75 to 70 per cent. The action of the thyroid gland was abnormal in 57 per cent. While it is difficult to trace exactly the results of disturbance in these various glands, an interesting experiment has been made by injecting placental extract into some of these bodies and observing the characteristic changes followed resembling those in pregnancy. It is believed that the fetal element in the placenta are the cause of the disturbance in these glands. While these researches do not suggest medical treatment, they are useful in giving information concerning the function of the glands.

Diagnosis and Treatment of Some Diseases of the Endocrine Glands. Murray,²⁴ in considering the thyroid gland, draws attention to the diagnosis of the condition of this gland by inspection with a good light. As this procedure is part of the examination of every pregnant patient, if carefully made, the writer's observations are of practical value. Where the thyroid is uniformly enlarged, the swelling in the front of the neck retains the normal shape of the gland, the right lobe being usually larger than the left. If the patient is asked to swallow, the large thyroid will rise and fall with the larynx and trachea. Should the tumor not be thyroid, but a ductless gland, a lipoma and basis of a sebaceous cyst, it may be adherent to the larynx and trachea and by moving with them simulate a goiter. If the goiter be firmly fixed to surrounding structures it may be prevented from moving. This is seen in malignant goiter or where there has been chronic inflammation. In young women it is not uncommon to find slight uniform enlargement of the thyroid and the modern fashion of wearing dresses which leave the front of the neck exposed to view has made observation upon this point comparatively easy. It cannot, however, be known that such enlargement is more frequent than in former years. It must be remembered that an apparent fulness in the front of the neck may be caused by two parallel creases in the skin crossing the front of the neck at the level of the upper and lower poles of the lateral lobes of the thyroid gland with a layer of sub-

²⁴ British Medical Journal, November 27, 1920, p. 807.

cutaneous fat lying between. Such a condition, however, extends laterally behind the limits of the gland and does not move with deglutition. Upon inspection, irregularity in the outline of the thyroid and the distention of the veins would become evident. The front of the neck can be palpated except in very fat persons and usually the size of the thyroid can be fairly well made out. Percussion is not often employed, but is sometimes useful to determine the position of the trachea with reference to the tumor. If the thyroid becomes infected, percussion may give useful information and the writer describes a case in which a cystic goiter became infected by the *Bacillus coli communis*, with the formation of gas where the percussion resonance was obtained. Incision and drainage confirmed the diagnosis.

Where a goiter is very large it may not compress the trachea, but may hang down upon the upper part of the chest. In some cases examination of the thyroid by the *x*-ray is necessary.

When an effort is made to estimate whether the action of the thyroid gland is deficient or excessive it must be remembered if the action of the gland is excessive there will be increased metabolism of the tissues which may produce signs of exhaustion. The pulse-rate is increased and there is tremor in the muscles, mental depression and palpitation of the heart. By Sandiford's method, employed in the Mayo Clinic, the metabolic rate can be determined, and this is of importance in estimating whether the patient has a genuine condition of the thyroid or a neurosis simulating it. Observations usually show that after rest or after the removal of the thyroid a distinct gain in the condition of the patient can thus be clearly demonstrated. Where hyperthyroidism is present, radium or the *x*-ray have been used to advantage, and rest in bed, a liberal diet of milk, fats and carbohydrates may also be of value. Red meats and meat extracts should be avoided, as they tend to stimulate the secretion of the thyroid. The use of a mild faradic current an hour twice a day is sometimes useful. Arsenic, given in small doses for several months, has yielded good results. The writer states that no constantly good results have been observed after the use of organic extracts, with the possible exception of the suprarenal gland. The various preparations made from animals after thyroidotomy have not been useful with the exception of fresh milk from a thyroidless goat.

The thyroid gland and its functions are of special importance to obstetricians because the thyroid has a considerable part in the functions of the reproductive organs. Thus sterility and obesity are lessened by the administration of thyroid extracts, the secretion of breast milk is increased and in some instances a toxic condition during pregnancy may be lessened. On the other hand, hyperthyroidism or toxic goiter is a distinct variety of the toxemia of pregnancy. In pronounced cases a general effect of this condition upon the circulation and breathing of the patient may be so bad as to jeopardize the patient's life during labor. In the worst of these cases the advent of uterine contraction greatly disturbs the action of the heart and respiration, and the patient may be threatened with suffocation. The gland actually enlarges at this time.

The writer at one time had under his care a woman suffering from

hyperthyroidism who had lost one child in a distressing and dangerous labor. During the next pregnancy she was kept in the best possible condition and brought into the hospital in the last month of pregnancy. Here, when labor began, symptoms became so threatening and her distress so great, that she was at once delivered by section. Mother and child recovered well and the mother was subsequently relieved by the removal of the thyroid. A similar experience, in which the symptoms were less distressing, and the immediate danger was less, occurred in a second patient. Both were delivered by section and both subsequently had the thyroid gland removed.

The pituitary gland can only be examined by the *x*-ray and it is difficult even by that means to accurately determine its condition. Considerable enlargement of this gland through pressure may cause temporal, frontal headache and disturbance of vision. When there is prolonged excessive action of the gland, acromegaly is produced in the adult and excessive overgrowth in young persons. While the *x*-ray may be somewhat useful in the treatment of acromegaly, it can do no more than palliate. When the secretion of the pituitary gland fails early in life there is arrest of development in the skeleton and other portions of the body, and this is produced principally through loss of function in the anterior lobe. In the posterior lobe diseased conditions may cause great increase in the subcutaneous fat without, however, a development of pain. The patient is unable to take large quantities of sugar without disturbing the general condition. The temperature is subnormal and the pulse is slow and of low tension. There may be excessive secretion of urine. This symptom can often be controlled by the hypodermic injection of 1 cc pituitrin every day or two. Some improvement may be caused by giving the dried gland in doses of 2 or 3 grains several times daily. It is recognized that pituitrin can raise blood-pressure in shock or heart failure and also stimulate the peristalsis of the bowel. Its action upon the uterus in doses of 10 to 30 minims, given subcutaneously, is well known, and in cases where shock is treated by intravenous saline transfusion, pituitrin may be added with advantage to the fluid employed.

In the suprarenal gland the cortex and medulla have different functions. The medulla produces adrenalin, a powerful stimulant to the sympathetic nerves; the cortex has to do with the development of the genital organs. There may be excessive activity or loss of function in these glands. It has been thought that overaction has been responsible for the high blood-pressure seen in some diseases of the kidney. When the glands are destroyed, usually by tuberculosis, Addison's disease results, a condition difficult to recognize in the beginning, but producing marked changes later on. While cases of recovery are on record, with those patients it is probable that one gland only was involved. Adrenalin is a well-known and useful remedy, and among its other effects has proved efficient in relaxing spasm of the esophagus.

The Use of Blood Transfusion in Obstetric Practice. This interesting subject is of special interest in view of the fact that the transfusion of blood is practised extensively in all branches of surgery and not infre-

quently in medical practice. It is necessary to give special attention to the phenomenon observed in obstetric cases where transfusion is performed. The blood of the parturient patient is essentially different from that of the non-parturient, and if this fact be neglected good results cannot be obtained.

An interesting contribution to this subject is made by Vago,²⁵ of the Obstetric Clinic in Buda Pesth. He states that it is the usage of this clinic to collect blood for transfusion, and especially from pregnant, healthy patients. This blood is defibrinated by shaking in sterile glass vessels and citrated by 0.02 per cent solution. Wassermann reaction is taken to be sure that syphilis is not present. All pregnant patients in the hospital, in such condition that they might be useful as givers of blood are examined, and their condition is recorded. In cases in which transfusion may become necessary in five or six hours the one selected to give the blood must be examined to determine whether there are elements in the blood which may do harm rather than good to the recipient. To lessen the danger of anaphylaxis, blood is kept an hour in a thermostat at 39° C. Before the transfusion the blood is filtered through eight layers of gauze, thoroughly shaken so that the serum is oxygenated and thus will convey an increased quantity of oxygen to the recipient.

The reinfusion of blood taken from an individual can be accomplished after it is defibrinated, filtered and warmed. To perform transfusion a sterile irrigator is usually first employed, later the glass cylinder used in giving salvarsan. Into this first was placed the blood at a temperature of the body and later physiological salt solution at body heat. The contents of both cylinders were connected by a glass T-tube and a rubber tube so arranged that the percentage of each could be regulated as the fluid entered the vein of the recipient. The cubital vein of the recipient was selected and warm salt solution at first introduced, followed by the blood mixture. During the transfusion a salt solution was constantly employed in irrigating the area of transfusion. The quantity, from 1 to 1½ liters, could readily be introduced by this apparatus. Where smaller quantities were desired, 50 to 200 cc, the piston syringe with a cannula was arranged so that the stream could be directed to either the recipient or the reservoir. When anemia was acute, the blood employed was given in the vein; when the anemia was but slight, the blood was put into the rectum; when there were contraindications to the venous methods, the fluid was injected into the substance of a muscle. Special precautions must always be taken in transfusion to avoid thrombosis and air embolism. Thrombosis may result if the blood is not properly defibrinated and if care is taken to prevent any small pieces or clot which may have formed in the tubes of the apparatus from entering the circulation. It is usually sufficient to defibrinate blood if it be shaken thoroughly for ten minutes in a sterile glass vessel. After the blood has been defibrinated, it should be filtered before its administration.

To prevent air embolism strict attention must be given to the technic

²⁵ Zentralblatt f. Gynäkologie, 1920, No. 39.

of the procedure. Air must be expelled from the tubes before the transfusion is undertaken, and when the cannula is inserted it must be while the salt solution is running in full volume. In patients in whom there is a previous disposition to embolism or thrombosis, as patients suffering from arteriosclerosis or thrombophlebitis, intravenous transfusion is contraindicated.

In the experience of the writer the transfusion of blood is indicated in acute anemia following internal hemorrhage in ectopic gestation or postpartum hemorrhage after delivery.

In the chronic anemias resulting from excessive uterine hemorrhage or bleeding from the ovaries, hemorrhage from uterine fibroids or cancer or hemorrhage in hemophiliacs, transfusion is also indicated.

In septic infection this procedure has been recommended and tried by some, with the hope that it would promptly increase the resisting power of the patient's blood, and therefore rapidly lessen the violence of the infection. In 30 cases of extra-uterine pregnancy without mortality the writer found it necessary to resort to intravenous transfusion in 3 only. The first was that of a patient in shock, with pulse 160. Operation was done under local anesthesia; intravenous transfusion of 500 cc of defibrinated blood, with saline solution to make 850 cc was given. Prompt improvement followed; fourteen hours after the transfusion the hemoglobin was 45 per cent, one week after the transfusion it was 56 per cent, four weeks after it was 76 per cent, with a corresponding increase in the red cells. The second case was treated in a similar manner, operation being done under local anesthesia, the transfusion being 600 cc of defibrinated blood taken from the abdomen of the patient, diluted with 300 cc of salt solution. Seventy minutes was occupied in the transfusion. The improvement was immediate and lasting. In the third case 200 cc of blood were taken from the abdominal cavity into which it had escaped after the rupture of the tissue. It was diluted with 200 cc of salt solution and was given intravenously while the abdominal wall was being closed. Immediate improvement followed. In these cases blood was taken from the abdomen, defibrinated and diluted with salt solution given by intravenous injection.

The writer employed the method in 24 cases of hemorrhage following delivery. Of these, 9 occurred because of the retention of cotyledons. In 1 case blood was taken from a pregnant woman in whom the Wassermann reaction was negative, defibrinated, diluted and injected. The result was exceedingly good. In a second case transfusion by defibrinated blood and salt solution did not prevent the rapid development and fatal issue of septic infection. The hemoglobin in this case was reduced to 30 per cent. The remaining cases did well.

It is the custom of the clinic in the delivery room to collect from the placenta and umbilical cord in healthy patients the blood at the time when the patient is delivered. This blood is kept in an aseptic condition, diluted with salt solution and is often mixed with 30 drops of tincture of opium and injected into the rectum of the patients suffering from anemia. Where it is not necessary to obtain a prompt result this method gives satisfaction. From 1 to 1½ liters is used, and this is given

by the drop method, requiring three or four hours' time. An interval of a day or two is often allowed between the giving of this blood.

In the chronic anemias following operation for a tumor or other conditions the method has also in his observation been satisfactory. Its use was not without complications. In 1 case in which the hemoglobin was 30 per cent, transfusion was followed by chill and a marked rise of temperature. This immediately subsided and the patient's further recovery was uncomplicated. In another case, during the transfusion, symptoms of air embolism developed, which lasted five minutes, and then subsided without further return. In menorrhagia blood was given by the bowel and also by intravenous injection, the latter followed by chill and fever. These symptoms rapidly disappeared and the patient went on to recovery.

In chronic anemia, especially good results were obtained by rectal injections of the prepared blood and blood fluid. In cases in which operation had been done for malignant disease, if a stump of malignant tissue remained behind, hemorrhage sometimes occurred from this tissue, following a transfusion.

The writer treated 4 cases of septic infection with a transfusion of blood. In 1 case marked improvement followed the employment of this treatment. In the others the improvement was more transient and the essential progress of the case was not materially altered.

His most successful result in sepsis was obtained in a case where infection of the blood stream by the hemolytic streptococcus developed after abortion. The patient received 50 to 100 cc of the blood mixture at intervals of three days by intravenous injection for some time. Three days after the last injection the daily chill became more infrequent and then ceased; the patient's temperature gradually fell to normal and recovery ensued. It is possible that in this case recovery might have occurred without the transfusion, but apparently the method of treatment was efficient. The question naturally arises whether the transfused blood remains in the organism as a foreign body, capable of performing its individual function, or whether it practically becomes the cells of the recipient. When the latter occurs, it is evident that the benefit resulting from the treatment will be of greater length and development than when such is not the case.

The writer believes that this method of treatment is useful: (1) In the acute anemias where it may save life; (2) in the chronic anemias by increasing the volume of the blood it may produce sufficient improvement to enable the patient to go on to further gain. The method of repeated dosage of comparatively small quantities seems to arouse the organism to increased function and to give a much better result than the administration of very large quantities at one time. The microscopic study of the blood under the preferred method shows that the blood cells take on a regenerative character and that a healthy development follows the injection.

In cases in which patients are anemic and greatly reduced before operation, and where it is desired to prepare them for an operation, this method may be of very great value. In cases in which the sudden intro-

duction of a considerable quantity of blood would raise the pulse tension to a high point, hemorrhage might result from areas of diseased tissue. This is sometimes seen in cases of cancer or of ulcer where the hemorrhage has come from the parenchyma of diseased organs. Under such conditions care should be taken in limiting the quantity of fluid used.

When patients show a tendency to recurrent hemorrhage and there is no distinct anatomical lesion to be found from which the hemorrhage can come, injection of defibrinated blood from a pregnant patient may often result in controlling the hemorrhage. This is especially true in cases in which there is reason to suspect that failure in the glands of internal secretion has been responsible for the bleeding. It is interesting to observe that in 5 cases in which intravenous transfusion was done, and where the blood from a pregnant woman had been used, that in the recipient injection was followed by very strong contractions of the uterus, and that hemorrhage, which had been going on for some time, ceased on the use of this treatment.

It was possibly contrary to what might have been expected to find that in septic cases intravenous transfusion of blood did not produce the beneficial result which had been hoped.

LABOR.

Labor Complicated by Rupture of the Uterus and Placenta Previa. Byers²⁶ reports a spontaneous complete intraperitoneal rupture of the uterus in labor, obstructed by contracted pelvis. The patient was immediately operated upon and a tear in the uterus, about six inches in length, was found on the posterior surface of the fundus down through the right lower uterine segment. The uterus was drawn over to the left side and laceration carefully sutured. The abdomen was closed without drainage. The patient made an uninterrupted recovery.

The case of placenta previa was in her fifth pregnancy, near full term, and the placenta was central, entirely covering the internal os. Two days after admission the patient had sharp hemorrhage and was immediately delivered by section. Mother and child made good recoveries.

As regards the choice of suture material the writer lays stress upon the method of preparation in the catgut used. In 39 Cesarean sections, 30 had tanned sterile catgut employed, and there has been 1 death. The patient was septic before admission. Three cases have been operated upon twice and 1 three times. Four have delivered themselves spontaneously in subsequent pregnancies.

Labor Complicated by Prolapsus of the Cord. Zweifel,²⁷ in over 25,000 births, reports prolapse of the cord in 165 cases after rupture of the membrane, or 0.5 per cent. The presentation was transverse in 10 per cent, pelvic in 5 per cent and vertical in 0.4 per cent. This occurs most frequently in women above the average age; evidently any presentation which does not completely fill the lower uterine segment makes this

²⁶ British Medical Journal, August 7, 1920, p. 202.

²⁷ München. med. Wehnschrift., 1920, No. 3.

impossible. High insertion of the placenta, pelvic contraction and prolapse of the arm also predispose to it. In 119 cases in which the child was living at the time of the prolapse, 45 per cent were born dead. In general the fetal mortality may be given as 37.5 per cent.

Balard²⁸ has collected several cases in which the child was born living and survived, although the cord prolapsed and had ceased to pulsate. When the cord prolapses the fetal heart should always be examined by auscultation, and in some cases, although the heart sounds cannot be heard, the fetus may still survive. When there is the least doubt concerning the life of the child, the obstetrician should not perform a mutilating operation, but should endeavor in every reasonable way to extract the child alive.

Tumors Complicating Labor. Spender²⁹ bases his paper upon notes of 37 cases. The study shows that in a large number of patients having small tumors pass through pregnancy and labor without difficulty and that tumors as large as an adult's head may occasion no difficulty.

Eight of the writer's cases illustrate this fact and a pedunculated reniform tumor may rotate and become strangulated, causing inflammation. Three cases of retroversion and retroflexion of the uterus produced by fibroids, 1 of acute anteflexion and 2 of inversion of the uterus, are described. In 7 cases submucous tumors were removed after childbirth or miscarriage by enucleation through the os uteri. Sepsis occurred in these cases, but the patients recovered without hysterectomy. There were 3 fatalities: 1 from occlusion of the ileum by 2 pedunculated subperitoneal fibroids; 1 from subperitoneal reniform tumor which became twisted and infected; 1 was infected and died of acute sepsis after Cesarean section. In some of these cases the patients had been followed after operation as long as twenty-five years. Fibroid tumors complicating pregnancy are thought to occur about once in 150 pregnancies.

Ectopic pregnancy is rare among these cases; placenta previa occurs with unusual frequency. Pain or tenderness over the tumor or uterus are frequent symptoms, especially in necrobiotic tumors. The pain is usually relieved by rest, light diet and anodyne. Where torsion or inflammation or infection of the tumor occurs the symptoms are acute and operation should be done promptly; such tumors may cause pressure on veins resulting in edema, albuminuria and ascites. Abnormal presentations, especially the breech, are frequently observed.

In spite of the fact that many of these patients are not young, labor is often spontaneous, and as the tumor is drawn up out of the way during labor the use of forceps may be required and the placenta or decidua may be retained after labor; while abortion is not especially frequent, premature and postmature labor are not uncommon.

Diagnosis may be difficult in these cases. The great majority of cases require only careful supervision during pregnancy. Induction of abortion and premature and forcible delivery through the vagina are contraindicated. Forceps, craniotomy and embryotomy are rarely

²⁸ Arch. mens. d. obst. et de gynec., 1919, No. 8, p. 245.

²⁹ British Medical Journal, February 7, 1920.

needed. Polyps and pedunculated subperitoneal tumors should be removed.

Vaginal myomectomy may be required for cervical fibroids but not for retrocervical. Abdominal myomectomy is rarely needed only for very much twisted and necrobiotic tumors. Abortion and hemorrhage are liable to follow operation requiring hysterectomy. The tumors should be examined bacteriologically before operation, and if infected the whole uterus should be removed. Hysterectomy and myomectomy during early pregnancy are, the writer believes, much too commonly performed. Conservative Cesarean section is sometimes indicated, especially if fibroids are associated with contracted pelvis and malpresentation of the child, especially in elderly primipara. It is sometimes possible to remove a myoma and child through the same incision.

In the *British Medical Journal*, February 21, 1920, p. 246, Spencer continues his discussion of tumors complicating labor and gives the results of 55 patients, pregnant, submitted to ovariectomy, with 1 death; this happened in intestinal obstruction caused by adhesions of the coil of small intestines in the stump of ovarian pedicle. The abdomen was opened and the coil was separated, but the patient died. The treatment of ovarian tumors complicating pregnancy must be selected after consideration of many factors. Experience shows that, so far as the child is concerned, the mortality is higher with operation than without. The writer believes that operation has been done too frequently in these cases. During the first half of pregnancy many of these tumors need not be mutilated; during the second half a large ovarian tumor, ruptured, inflamed and strangulated, should be removed. Small tumors easily pushed up should be watched, and, if any bad symptoms develop, should be removed at the end of pregnancy or toward the end of the first stage of labor or after delivery. Small tumors low down in the pelvis may be watched and removed at the end of pregnancy or toward the end of the first stage of labor. If tumors are adherent or solid, Cesarean section is indicated. In all ovariectomies during pregnancy, the vessels of the pedicle should be tied separately; the pedicle should be tied as far as possible from the uterus, and morphine should be given for the first two or three days after operation. In large tumors complicating labor, abdominal ovariectomy should be done at the end of the first stage, or in cases of small tumors after delivery. When operation is performed at the end of the first stage, a second operator may deliver the child by forceps when the tumor is being removed. If the tumor is incarcerated in the pelvis and cannot be pushed up in the Trendelenburg position, the uterus should be withdrawn from the abdomen in order that the tumor may be dealt with. Solid and adherent tumors in the pelvis may make Cesarean section necessary, but this should not be performed for cystic non-adherent tumors. When labor has advanced and the tumor is impacted in the pelvis, it may be best to deliver the patient by the natural passage after evacuating the contents of the tumor by incision and packing the cyst with gauze; but, if possible, the tumor should be removed within twenty-four hours, preferably through an abdominal incision. When tumors are not adherent, vaginal ovariectomy may

be performed, but in this there is greater danger from hemorrhage, difficulty in safely tying the pedicle, necessity of cutting up the tumor, impossibility of examining the other ovary and also danger from the presence of the vaginal wound.

Induction of premature labor, forceps, version, and simple tapping of a cyst as a means of overcoming dystocia of the ovarian tumor are absolutely contraindicated. Ovarian tumors should be removed as soon as possible, at least within twenty-four hours of delivery. If septic inflammation of the uterus is feared, a delay of a week or two may be advisable unless indication of strangulation or infection of the tumor arises, when operation should be done at once.

In the *British Medical Journal*, March 6, 1920, p. 320, Spencer discusses labor complicated by cancer of the uterus. He had 10 cases, and these and other statistics show that cancer of the uterus complicating pregnancy is not common. Wertheim, in 250 cases of cancer of the cervix, found only 6 complicating pregnancy. Cases may be divided for treatment into operable and inoperable and also those in which the child is or is not viable. The question of operation is usually decided by the presence or absence of fixation of the uterus and thickening of the tissue in the parametrium. In late pregnancy, the interest of the child and the large size and vascularity of the uterus increases greatly the danger of the operation. These cases may be treated by high amputation, vaginal hysterectomy, extended vaginal hysterectomy, abdominal hysterectomy, extended abdominal hysterectomy and combined vaginal and abdominal hysterectomy. Radium and the x -ray are also used in cancer of the cervix complicating pregnancy. Radium is the chief agent aside from operation, and it is not yet determined whether this may or may not injure the fetus.

In early pregnancy, operable cases should be operated on at once. The best results are obtained by the Wertheim operation. In feeble or fat patients, vaginal hysterectomy, preferably with the cautery, may be selected. When the cancer is squamous carcinoma, amputation of the cervix may be sufficient, especially if it is desirable to preserve the life of the child and fertility of the mother. During labor or abortion the same operations are indicated if the patient is not infected; but, if infected, the entire uterus must be removed. When cases are inoperable and not complicated by bleeding or infection, patients should be kept at rest and the Porro operation performed when pregnancy has advanced. During labor or abortion the case should be treated on general principles to prevent infection, and during the puerperal period the cautery, radium and the x -ray are useful. In late pregnancy operable cases should be treated by Cesarean section followed by extended abdominal hysterectomy. If the patient is feeble and the growth infected, it might be well to remove the cervix by a cautery, then remove the child by the vagina or abdomen and apply radium with, or without, the removal of the uterus. This would be safer for the mother than abdominal Cesarean section while the removal of the uterus would involve some increased risk to the child.

Vaginal Cesarean section involves too great a risk, and there is no recorded case where this has been followed by cure.

During labor the risk to the patient is greatly increased; in early labor, Cesarean section, followed by abdominal hysterectomy, is best. If labor has advanced and the growth is not large, it may be safer to deliver the patient through the vagina, and afterward, early in the puerperal period, to treat the disease by one of the methods described. Five of the 7 cases cured were operated on after delivery. Inoperable cases should be treated by the Porro operation with the use of the serrenœud. It has the advantage over the conservative Cesarean section in that it removes the placental site from risk of infection, and over Cesarean hysterectomy with peritoneal stump treatment it also has the advantage that infectious discharge can readily escape by the side of the wire, which can be placed on any height above the growth, provided the placental site be removed, in case of a dead or decomposed child, by the Porro method, above the ring of the uterus before the body of the organ is opened or amputated.

During the puerperal period the treatment is practically the same. Three cases of high amputation have remained free from recurrence for twenty-five, twenty-two and nineteen years. As far as records show but 2 other cases of cancer complicating pregnancy have remained well for five years after operation, 1 by Olshasen, five and three-quarter years, and 1 by von Ott, eight and a half years. Both were operated on by vaginal hysterectomy in the puerperal period. Two additional cases have been cured, both five years, which were operated on by extended abdominal hysterectomy.

The writer believes that the use of the cautery in 2 of his cases, antiseptic douches, and the fact that operation was performed after delivery, when the patients were involuting, were all important.

Artificial Rotation of the Head in Persistent Occipitoposterior Position Complicating Labor. Lackey³⁰ believes that of 5 of such cases 4 are treated by spontaneous rotation. If this be done, an absolutely accurate diagnosis must be made, and an anesthetic may be necessary for this purpose. If progress is being made, however slow, interference should not be practised, but if the head remains high and the pains are weak, the whole hand should be introduced beyond the head, the membranes ruptured, the fingers reaching a shoulder, and rotate the whole child on its longitudinal axis with the help of the left hand if necessary. After allowing a short time for molding of the head, forceps are applied and the child is easily delivered. More often the position is not diagnosed until the head is more or less fixed at the brim or at the cavity of the pelvis; it is useless to promote flexion by pressing upon the head during pain, as the head must be rotated into the anterior position with one hand while the other, acting through the abdominal wall, attempts to rotate the shoulders; if this fails, forceps should be applied, pushing back the head gently and the handle carried around in a large circle. As the occiput occupies the anterior position, it should be fixed by slight traction to prevent it from returning to its abnormal position. The forceps should then be removed and again applied for traction. During

³⁰ Edinburgh Medical Journal, March, 1920.

rotation there should be no traction and every effort should be made to rectify the abnormal position before applying force. The writer has found the method described a safe one and giving excellent results.

Rupture of the Vagina Complicating Labor is described by Palmer³¹ in 2 cases admitted to the London Hospital. In 1 a large child had been born with the difficult use of the forceps: the perineum was torn and in an effort to remove the placenta the physician's hand was passed into the abdominal cavity, where he found the placenta. At the hospital the uterus was found almost completely separated from the vagina, except for a narrow border in the region of the left uterine artery and a small portion of the anterior wall of the cervix close to the bladder. There was much free blood in the peritoneal cavity. The uterus was removed as rapidly as possible and the patient made a good recovery.

The second case, a multipara treated by a mid-wife, and after good pains for fifteen hours they became different in character from the preceding ones. There had been no manipulation and only one vaginal examination. On the right of the fetus was a hard tumor about the size of a fetal head, thought possibly to be a fibroid. A moderate use of the forceps failed and the child was delivered by craniotomy. The tumor was found to be the contracted uterus, and the child had been lying in the abdominal cavity, from which the placenta was removed. On section, there was a large T-shaped tear in the posterior vaginal wall and much blood in the peritoneal cavity. The uterus was rapidly removed and the patient made a good recovery.

In discussion it was stated that rupture of the vagina, with rupture of the lower uterine segment, is much more common than is generally believed. Sections from the lower uterine segment in patients who had died undelivered during obstructed labor showed how greatly the vagina is stretched and drawn up by the uterus during obstructed labor.

Quinine as a Stimulant in Labor. Acton³² quotes the results observed by physicians practising in the tropics, where quinine must frequently be given for malarial fever and often to pregnant patients. The majority of opinion is that alkaloids of cinchona have no fixed and definite influence in causing contractions of the uterus. When these substances do produce contractions, the result depends upon an idiosyncrasy of the patient, and cinchona and its derivatives should be used during pregnancy with caution, because of its uncertain and possible effect in stimulating the uterus. In malaria, quinine may have a useful function in preventing the death of the fetus, regulating the high temperature of the mother and therefore preventing interruption of pregnancy.

Acton experimented with preparations of quinine upon the uterus of warm-blooded animals and found that, in certain concentration, quinine caused contraction of both longitudinal and circular fibers of the uterus, the effect produced depending upon the concentration of the solution; weak solutions of 1 to 300,000 have no effect; under certain conditions 1 to 150,000 produce contractions, while 1 to 44,000 produce a tonic

³¹ British Medical Journal, May 1, 1920, p. 602.

³² Lancet, January 29, 1921, p. 216.

spasm which would cause asphyxia of the fetus from constriction of the placental sinuses. When quinine is given the degree of concentration of the blood varies with doses taken, while the susceptibility of the individual depends upon the rate of absorption. Weak and anemic persons are most powerfully affected by quinine. When large doses, represented by a concentration of 1 to 150,000, are given, immature uterine contractions are made strong, and, if the conditions are favorable, labor might be brought on.

In malarial cases the mother's temperature should be kept not higher than 103° by sponging, and, if necessary, quinine in some form, from $2\frac{1}{2}$ to 5 grains in malarial cases, may be given every two to four hours, and so far as malaria is concerned 20 grains a day is sufficient to control the disease. The patient should be completely at rest in bed, and, if there is excitement, an opiate should be given.

Muschallik,³³ in the Breslow Clinic, has used quinine to bring on labor by intravenous and intramuscular injections. He treated 50 cases in which labor pains were deficient by this method. In one-sixth of the cases systematic and cramp-like labor pains developed; in 12.5 per cent it was necessary to terminate labor by some obstetric operation. A 5 per cent solution of hydrochlorate of quinine was used; 1.0 cc of quinine was sterilized in 20 cc of sterile water and dissolved, and of this 10 cc were injected into the cubital vein and shortly afterward 10 cc were injected into the gluteal muscles. The best results were obtained in cases in which the membranes had ruptured prematurely; labor pains developed and the cervix was not shortened. Labor pains often came on in five minutes after injection and labor terminated in about eight and a half hours.

There were 17 cases in which the method was used for secondary failure of uterine contractions. In some of these pituitrin was employed in contrast with quinine. There seemed to be a marked difference in the reaction of patients, as some reacted much better to pituitrin and others to quinine. In the 17 cases, 7 were terminated by some obstetrical operation. This method was fairly successful in 35.3 per cent of cases, while the percentage of operations was 41.1. In 5 cases of premature labor in which labor had begun and then ceased and the uterus was not acting, quinine produced no results. In 4 cases in which labor was in active progress, quinine strengthened the pains. It was found impracticable to employ this method when the placenta was retained, as the preparation and use of the drug and its uncertain workings made it unreliable. The writer sums up his experience by saying that in 50 cases of primary uterine inertia positive stimulation of the uterine contractions was obtained in 42 per cent and failure in 58 per cent. No symptom indicating danger to mother or child developed and the ringing in the ears, disturbance of vision and sensation of heat and bitter taste produced no serious results. Uterine pains were never sufficiently strong to jeopardize the child, although such pains introduce an element of great uncertainty and their ultimate effect cannot be foreseen. The best results were

³³ *Monatschrift f. Geburtshülfe*, 1920, vi, No. 52, 378.

obtained in primipara in whom labor had begun and then had subsided. The writer believes that quinine given by the mouth acts more efficiently than intravenous and intramuscular injections. He believes the best results would be obtained by giving quinine by the mouth and pituitrin by hypodermic injection.

Rupture of the Uterus in Labor. Anderson³⁴ reports an extraordinary experience in which recovery followed rupture of the uterus treated by gauze-packing. A primipara had been delivered, outside the hospital, of a four months' fetus which presented by the feet. The attending physician discovered a tear of the cervix extending downward on the left side. He removed the placenta with the fingers and found the intestines in the uterus. The writer first saw the patient fourteen hours after delivery, when she was in extreme collapse, with oozing hemorrhage, uterus relaxed and the cervix contracted. Under anesthesia a transverse tear of three or four inches was found across the fundus and a coil of large intestines in the uterus. The tear on the left side of the cervix did not connect with the tear in the fundus. Under anesthesia the patient was placed in the Sims' position with the pelvis raised; the prolapsed bowel was replaced and the uterus was stimulated to contract by pressure and packed with sterilized gauze. This was replaced in thirty hours and a second packing removed thirty hours later. The patient was given pituitrin, morphine and saline solution by the rectum and vaginal douches of lysol and inhalation of oxygen. Swelling and tenderness developed in the left iliac region; the lochia was offensive and there was fever. The patient gradually improved and insisted on leaving the hospital twenty-five days after admission. A pelvic abscess afterward developed and was opened, but two months later the patient was well. It was thought that the tear in the cervix complicated the patient's recovery and was possibly the site of infection. Operation was not attempted because of the patient's very serious condition, but the treatment employed gave exceptionally good results.

Attention is called to Spencer's report of 4 such cases successfully treated by packing with iodoform gauze. In discussion, it was thought that packing should be reserved for cases which ruptured in the broad ligament or cases in which lacerations had not extended to the peritoneum. A similar case was reported in which a mass of intestines protruded through the vulva; this also was treated by replacing the bowel and packing with gauze. The patient recovered and subsequently had two children successfully.

Bourne reported a spontaneous rupture of the uterus following pituitrin. The patient was in her twelfth and tedious labor. The cervix was fully dilated, with the head on the perineum. One-half cubic centimeter of pituitrin was given hypodermically; and hour later violent pains developed, the patient collapsed, the head receded and the pains ceased. When admitted to the hospital she was in a profound shock, so that operation was impossible, and an attempt was made to empty the uterus by perforating the head and cutting through the neck; the

³⁴ British Medical Journal, January 19, 1921, p. 829.

patient failed rapidly and died. At autopsy, the trunk of the child and placenta were found in the abdomen and there was a tear five inches long in the uterus, beginning in the lateral wall and lower segment and extending downward and inward to the cervix.

Other cases were reported in which the uterus had ruptured after pituitrin was given before dilatation was complete; but in Bourne's case the cervix was fully dilated and the head was on the perineum. Attention was also called to the danger of giving pituitrin before introducing bougies to produce labor. In four autopsies on infants, tears of the tentorium cerebelli and cerebral hemorrhage were found in children born by precipitate labor following the use of pituitrin.

The Transfusion of Blood Following Complicated Labor. Considerable attention has recently been given to the transfusion of human blood in parturient patients. Bumm³⁵ had tried the transfusion of blood taken from abdominal ectopic gestation in 13 cases, average quantity 670 c. c. In 2 cases chill and fever followed; 1 patient died in the beginning of the transfusion and others seemed benefited by it. Eleven cases received transfusion from blood of a relative or husband; here the average quantity varied from 600 to 1200 c. c. In 5 there was no reaction; in 6 chill and fever. Six cases received blood from individuals not related; 4 of them had rise of temperature, 2 had none. Blood from an eclamptic was employed in 19 cases in small quantities up to 1000 c. c.; 10 had chill and fever, and in 1 the rise of temperature continued for three days, with malaise, headache, hemoglobinuria and icterus. Eight cases showed no symptoms of poisoning, convulsion or eclamptic symptoms or alteration of the urine in these cases. The writer believed that it is best to use, if possible, the blood of the patient if this has been poured into the abdomen through rupture of ectopic gestation. The writer alludes to the extensive literature on the question of blood transfusion for various conditions. In 13 cases of ruptured ectopic gestation, transfusion was practised in 9; the result at the end of the operation was surprisingly good; 3 showed disturbance of pulse and respiration, but after 500 c. c. were given the patient was so much improved that the critical point was evidently past.

Six cases of placenta previa with severe postpartum hemorrhage were treated by this method; 2 of these patients died, and the comment is made that it would have been better if the time spent in blood transfusion had been utilized more efficiently in checking hemorrhage. More brilliant results were obtained where the hemorrhage had ceased and where the heart action was very weak.

The writer also employed this method in cases of puerperal sepsis and was disappointed in the result; no improvement whatever could be observed.

Esch³⁶ draws attention to the danger of this method. He employed it in the pernicious anemia of pregnancy, with the hemoglobin reduced to 18 per cent. Three injections of blood were given into the muscles without producing improvement; 165 c. c. of defibrinated blood were

³⁵ Zentralblatt f. Gynäkologie, 1920, No. 12, p. 296.

³⁶ Ibid., March 27, 1920, No. 13, p. 321.

given in a vein. This was followed by restlessness, chills and fever and collapse, from which the patient was resuscitated with difficulty. Some improvement followed this and on the following day the patient gave birth to a macerated child, and died seventy-two hours after labor, four days after transfusion. At autopsy on the child's body, punctate hemorrhages were found in the lower lobes of the lungs, and bloody fluid in the pericardium and pleural cavities.

Nurnburger³⁷ has had experience with blood prepared with citrate of sodium. He has experimented upon animals to determine the quantity of citrate of sodium which it was safest to introduce into the circulation. The usual dose of 1 gm. of citrate of sodium to 100 cc of blood is, the writer thinks, too much. He would advise 0.2 gm. of sodium citrate to 100 cc of blood. Better results still are obtained by using 0.9 per cent of salt solution and 1 per cent of sodium citrate in from 200 to 500 cc of blood.

Induction of Abortion. Phillips³⁸ describes the induction of abortion as the interruption of pregnancy before the viability of the child. He divides the term "abortion" into the embryonic, occurring before the twelfth week, and fetal, taking place from the twelfth to the twenty-eighth week. In his paper he embraces both terms under the term "abortion."

In the thirty-five years of private practice he has done therapeutic abortion in 57 cases. In 18, the reason was the occurrence of what he terms "acute albuminuria;" in 2, glycosuria; in 11, uncompensated cardiac disease; in 15, incoercible vomiting; in 1, acute salivation; in chorea 1; placenta previa 6; cancer of the breast 3. A consultation was held upon each case and a complete agreement was reached that therapeutic abortion was the only justifiable procedure. Under modern conditions he would not include pelvic deformity as a justifiable indication for the production of therapeutic abortion.

In the cases of albuminuria the patients had the usual symptoms, and, in addition, 2 showed signs of mental instability. All were treated in the usual manner by rest, diet and drugs, but they did not grow better but rapidly worse. Convulsions occurred in none. Albuminuria disappeared in fourteen days after the operation in 12 cases. In the remainder albuminuria was present for some weeks. In 3 of the patients extensive changes in the teeth had occurred and in 3 others the placenta, when examined, showed areas of thrombosis.

In the cases suffering from glycosuria, the symptoms rapidly became more pronounced. Emaciation and thirst were the marked symptoms, with sordes around the mouth and a red tongue. Pregnancy seemed to stimulate the formation of sugar. Both cases were carried on until the end of the fifth month, when it was found unsafe to allow the pregnancy to go further.

In the writer's experience, it is very difficult to decide when to interrupt pregnancy in uncompensated cardiac disease. Dyspnea, edema of the feet, slight albuminuria, duskiness of the face and purplish color

³⁷ Zentralblatt f. Gynäkologie, 1920, No. 27, p. 720.

³⁸ Lancet, February 5, 1921, p. 266.

of the lips were present in these patients before the completion of the fourth month. Some of these cases were invalids before the pregnancy began. In 4, there was double aortic disease, aortic and mitral stenosis in 5 and mitral regurgitation in 2. The symptoms were relieved in all by the operation. A fatal result occurred, however, in 4 cases after from twelve to fifteen months.

The writer describes what he calls "incoercible" vomiting as one of the commonest reasons for the production of abortion. Nausea and vomiting began with these cases before eight weeks of the pregnancy had passed. The disease proceeded rapidly, and it was usually necessary to interfere before the twelfth week. A slightly rising temperature at night, a peculiarly anxious look in the face, rapid emaciation and a tongue dry and reddish were significant symptoms. Within a week of the operation the disease disappeared in 9 cases. In the remaining 6 it did not cease in a mild form until menstruation returned. In all of these patients every sort of treatment was tried, including the application of strong tincture of iodine to the cervix and the use of cocaine in the form of pessaries or suppositories inserted within the vagina. The writer believes that delay is dangerous in these cases. Three of them would have done much better had the operation been performed a week earlier. All were under thirty years of age and primigravida except 2, and in them the operation was done twice for the same condition. In 5 others pregnancy again occurred, but interference was not practised, although the patients were quite ill. In 6 of the 15 there was slight albuminuria, and in 2 cases there was old hemorrhage present in the decidua, but in the others no pathological condition could be found. The uterus was anteverted to a greater or less degree in 12 cases. In 3, there was retroflexion. In 2 of these the insertion of a pessary, with replacement of the uterus, failed to relieve the symptoms. In 1 case after the first pregnancy anterior suspension of the uterus was performed, but without relieving the patient.

It is well known that salivation to a greater or less extent usually accompanies nausea and vomiting in pregnant women. It rarely is severe. The writer, however, describes the case of a patient, aged thirty years, of highly nervous temperament and in her fourth pregnancy who had good general health. Her first pregnancy was normal; a parovarian cyst was removed at the third month in the second and salivation commenced and continued throughout the pregnancy. Salivation also complicated the third pregnancy, which ended in abortion. The fourth pregnancy was complicated by salivation throughout and the confinement was rapid and easy. In the fifth pregnancy more than two quarts of saliva were secreted in twenty-four hours. There was nothing abnormal in the saliva except excessive water; no albumin was present. The uterus was retroflexed, replaced and supported by a pessary, but without benefit. There was sleeplessness, rapid loss of flesh and mental disturbance, which made interruption necessary at the tenth week of gestation. Salivation continued two weeks after abortion and returned at each menstrual period for several months.

A primigravida, aged twenty-five years, had chorea at fifteen. In her

first pregnancy at three months she became violently ill, and at the eighteenth week had symptoms of acute mental disturbance. After the induction of abortion she rapidly improved, although for a year she had violent movements when excited. Six cases of placenta previa were treated by induction of abortion with a small de Ribes bag. In 3 cases in which a woman had had a breast removed for cancer it was considered unsafe to have the remaining breast stimulated by pregnancy. Accordingly, abortion was performed. While he does not advise this as routine practice the conditions in each case should be carefully investigated and treatment selected accordingly.

The writer places together two classes of cases which require careful consideration: pregnancy complicated by mental disease and pregnancy complicated by a retroflexed impacted uterus.

When mental disease develops in early pregnancy it is usually the result of exhaustion from emotional shock and anxiety or physical disease followed by insomnia. The writer classifies these into "border-line" cases where there was mental disturbance before marriage and where when pregnancy occurs definite symptoms develop. In the second class he places those who, healthy in all respects before marriage, since marriage have been subjected to severe nerve stress and develop mental symptoms on becoming pregnant. In the third class are those who are normal mentally and with a good family history, who, on becoming pregnant, develop an exhausting illness, such as chorea, uremia, obstinate vomiting or salivation, and begin to show signs of impending mental disturbance, of which they themselves are cognizant.

If pregnancy is to be interrupted at all in these cases, it should be done before the tenth or twelfth week; if interruption is delayed beyond this time, the patient's prospect of recovery is much lessened. It is usually necessary to use sedatives, with the exception of opium, freely in the treatment of these cases. Some have considered that a retroflexed pregnant uterus is cause for abortion, but unquestionably this is true only when the condition gives rise to grave symptoms imperilling the life of the patient. One must remember that in many of these cases the uterus is spontaneously reduced as pregnancy advances. It is on record that a patient has gone to full term and given birth successfully to a child while the uterus remained in this condition. The writer personally has never seen a case in which the induction of abortion was indicated, and the situation of the cervix pressed firmly into a edematous vaginal wall would render difficult the introduction of any instrument into the uterus. Should the necessity arise he would prefer to open the abdomen and lift the pregnant fundus out of the pelvic cavity. He had seen 2 cases in which a diagnosis had been made of an impacted ovarian cyst complicating pregnancy, and where, at operation, it was found easy to raise the pregnant fundus out of the pelvic cavity.

Some writers would induce abortion for phthisis, general tuberculosis, epilepsy, conditions leading to paraplegia and cases in which previous labors have resulted in the birth of congenitally deformed or mentally deficient children. The majority of opinion in England, according to the writer, is that pregnancy in no way accelerates the progress of

pulmonary disease, and that this is also true of general tuberculosis. If such is the fact, then pregnancy should not be interrupted.

When an epileptic patient becomes pregnant it would not, in the opinion of the writer, be advisable to terminate the pregnancy, because he is not of the opinion that pregnancy aggravates the epilepsy. The same is true regarding paraplegia. In regard to congenitally deformed and mentally deficient children, the writer cites the case of a woman who had a peculiar deformity of the fingers which she had transmitted to her children. As she was then pregnant the question arose as to whether abortion should be produced. This was declined and the child was born without deformity.

The writer considers the induction of abortion as attended by definite danger. These risks are septicemia, sapremia, septic peritonitis, deep laceration of the cervix followed by para- or perimetritis, perforation of the uterine wall, thrombosis and blood or air embolus. The operation may often be followed by a long period of ill-health without definite symptoms. The method of operating depends somewhat on the period of pregnancy, whether before the twelfth week or from the twelfth to the twenty-eight week. He believes that the dangers attending the operation are such that every precaution must be used, and that the former common custom, as he styles it, of producing abortion by the introduction of the uterine sound or by injecting tincture of iodine or other fluids is attended with the greatest risks and cannot be sufficiently condemned.

In early cases he would operate with the patient in the lithotomy position, pulling down the cervix and inserting several laminaria tents in the cervix or dilating the cervix rapidly with graduated bougies. With suitable forceps the whole mass of the embryo may usually be removed, he states, in one piece. If, on examination, there is suspicion that a portion of the ovum has been left behind, the finger should be passed to the fundus, to be sure that the cavity is emptied and that no second ovum is present. The operation may be completed by washing out the uterine cavity with one teaspoonful of tincture of iodine to a pint of water or swabbing it out with iodized phenol. Packing the uterine cavity with gauze he considers undesirable. He would prefer the injection of pituitrin or ergot at the end of the operation. He has found that gauze removed from the uterine cavity even twenty-four hours after the operation had an offensive odor. He would not perform curetting unless there seemed to be some pathological change in the ovum.

The more advanced cases he would begin with laminaria tents and then insert a specially-made small de Ribes bag, which not only brings on pains, but, in placenta previa, safeguards the patient from the results of hemorrhage. The writer knows of no more difficult vaginal operation than the removal of a sixteen to twenty weeks' pregnancy by means of ovum forceps after rapid dilatation. The fetus has considerable size and the head much enlarged, but the tissues are so soft that in delivering the fetus the head may be left behind. This cannot be grasped by an usual form of forceps. There may be much manipulation required, with increased danger of sepsis.

This interesting paper illustrates strikingly the difference in views

existing between obstetricians in various countries. The majority of American obstetricians, with the patient under anesthesia, would practice rapid dilatation and thorough curetting, and in many cases packing of the uterus with 10 per cent iodoform gauze. We have repeatedly removed such gauze forty-eight hours after its insertion and found it clean, almost dry and without odor. The use of ovum or placental forceps is unsatisfactory, and such an instrument can do considerable damage to the uterine wall or even to perforate the fundus. It is interesting to note that in cancer of the breast the writer in 3 cases interrupted the pregnancy. Evidently the pregnancy was undesirable, for otherwise the breast might readily have been removed and the pregnancy allowed to continue. With the history of cancer, if pregnancy were dangerous in its stimulation to the breast then the patient could not have nursed the child had the breast been allowed to remain and the pregnancy go on; but it is difficult to see why three pregnancies should be sacrificed for fear of the development of cancer in the breast.

Regarding the management of cases of impaction of the retroflexed uterus, very much can be done to aid and hasten the return of the uterus to its normal position by judicious treatment. The use of the knee-chest posture, rest in bed in the lateral position, keeping the bowels and bladder reasonably emptied and the use of antiseptic tampons, in the reviewer's experience, have been very successful in these cases. The reviewer shares in the belief that operation, if necessary, should be abdominal section unless the uterus becomes infected, when its extirpation may be demanded to save the life of the patient. It is difficult to see how anyone could be led to attempt the production of abortion in a uterus anteflexed, pregnant and bound down in the pelvic cavity.

Regarding what is termed phthisis and tuberculosis, opinion of the scientific world is not entirely in accord with that of the writer. His statement that pregnancy in no way stimulates the spread of tubercular infection is not borne out in the experience of many American obstetricians. The distinction must be made in these cases between a pregnant woman who becomes tuberculous and a tuberculous woman who becomes pregnant. The circumstances in life in each case are of great importance and the possibility or impossibility of obtaining proper hygienic and medical care. So, too, the question of multiparity is important. If a woman who has children may not elect the risk of a pregnancy complicated by tuberculosis, while one who is pregnant for the first time might even risk life or health to obtain a child. Furthermore, there are cases of tuberculosis complicating pregnancy where not only should the pregnancy cease, but the woman be sterilized by operation.

Morphine in Labor. Mellroy³⁹ presented a paper on this subject at the Section of Obstetrics and Gynecology of the Royal Society of Medicine, based upon her experience in hospital practice at Constantinople. These patients included several nationalities; the majority were primiparæ and the cases were not selected, but morphine was given in complicated cases, where there were unusual presentations, for disorders of nutrition.

³⁹ British Medical Journal, January 29, 1921, p. 159.

Where no complications were suspected, vaginal examinations were not made; douches were not used. Morphine sulphate was given hypodermically in the upper arm: the first dose $\frac{1}{6}$ grain and repeated doses of from $\frac{1}{6}$ to $\frac{1}{4}$ grain, at varying intervals, throughout the labor, according to the condition of each patient and her capacity to bear pain. There was no excitement nor mental confusion as the result of the drug. Patients slept at intervals and awoke refreshed. The progress of labor was hurried rather than delayed, and while in some cases uterine contractions seemed to be slightly less strong, this was more apparent than real. After some experience with the drug, it was given to shorten labor. Thirst was increased, restlessness was diminished, the third stage was not affected and there were no risks apparently with regard to the child. There was no postpartum hemorrhage and convalescence was helped by less fatigue and absence of shock. The constant attendance of the physician was not necessary and the results, on the whole, were very satisfactory.

In discussion, some had observed that if morphine be given within two or three hours before the birth of the child the child breathes more tardily and less vigorously than if the drug be not administered. Others preferred opium, in solid or liquid form, as being much safer than morphine, for morphine, if given repeatedly before labor in some cases, affected the child.

A Prognosis for Labor. Shannon⁴⁰ presented a paper before the Edinburgh Obstetrical Society giving the results of his study in estimating the relative size of the head and pelvis to make a prognosis in labor and to determine the best method of treatment. He had carried out this method in 316 cases of contracted pelvis. It is not enough to measure the pelvis, but what is important is the comparative size of the child's head and the pelvis, and the fetal head is the best pelvimeter. After the type of pelvis has been obtained by pelvimetry, the fetal head is pressed into the superior strait in accordance with the type of the pelvis. In flat pelvis, downward pressure should so be made that the sagittal suture will lay in the transverse diameter of the pelvic brim. If the occiput were posterior, the head is often in the oblique diameter and had to be changed into the transverse before pressure downward was made. If the best results were to be obtained in generally contracted pelvis the head was not always situated normally, and in pressing downward care should be taken to select that oblique diameter which would give the best mechanism of labor in accordance with the position of the body. Abnormal positions of the head were verified after the diagnosis had been made by palpation during Cesarean section, when the incision was made through the lower uterine segment. If the fetal head is pushed downward on to the superior strait carelessly, the lateral flexion of the head might occur, followed by impaction. The thumb should be laid flat on the outside of the symphysis and flush with its upper border, and pressure should be made downward and backward in that way. A full bladder and pendulous abdomen, especially in primiparæ, made the

⁴⁰ British Medical Journal, January 29, 1921, p. 160.

estimation of overlapping difficult. A loaded rectum, tumors or a placenta lying behind the fetal head would push the head forward, so that overlapping is exaggerated. When the occiput was posterior in generally contracted pelvis there was more overlapping than when it was anterior. The maximum amount of overlapping was not found at the center of the symphysis, but in generally contracted pelvis the thumb had to travel above this point to arrive at the seat of greatest disproportion, and this was especially well-marked where the occiput was posterior.

When the fetal head on pressure sank into the pelvis without overlapping, if the patient was in the first stage of labor, the case would be treated as normal and as spontaneous parturition was expected. When the head did not enter the brim readily and the overlapping was not flush with the outside edge of the symphysis pubis the case should be left to Nature, with the expectation that the disproportion will not be sufficiently great to prevent this spontaneous birth. If the patient is not in labor, it should be brought on, if such a condition be found, and the child has reached the thirty-sixth week of intra-uterine life.

Where there is a medium amount of overlapping, one may still hope for a spontaneous birth. Patients should be allowed to go on in a second stage, four, six, eight or twelve hours. Mother and child should be carefully watched and forceps applied cautiously should progress cease, and unless the head readily descends, pubiotomy is indicated.

When the fetal head bulges over the pubis so much that the overlapping will in many cases be seen and where the disproportion is so great that the top of the thumb, as it lies in position, is partly covered by the part of the head that overlaps, one cannot believe that the forces of labor can mould the head sufficiently to allow it to go through the brim of a contracted pelvis. If the child is alive and in good condition, Cesarean section must be done. Before a positive decision could be made, one had to ascertain by pelvimetry the type of pelvis, then study the consistence of the fetal head, observe the degree and variety of biparietal obliquity and study the position of the fetal head in the pelvis. One must also estimate the probable character of the expulsive forces of labor in a given patient.

Labor Complicated by Previous Interposition Operations. In solving the problem of prolapse, what are termed interposition operations, whereby the uterus is fixed between the bladder and the anterior walls of the vagina, are sometimes practised. Among these methods that of Schautasche has been extensively followed. Weber⁴¹ raises the question of what may happen to a patient in labor who has had this operation. The writer alludes to 13 of these cases. Among them are 2 where spontaneous abortion occurred between the second and fifth month; in 2 the uterus had to be emptied in early pregnancy because of the suffering which developed; in 1 the uterus was extirpated at five months and a dermoid cyst of the ovary was found to have developed on the right side; 3 had Cesarean section after the classical method, practically at term, and 1 had craniotomy, the child having already died.

⁴¹ Monatschrift f. Geburtshülfe, 1920, No. 53, p. 77.

In 2 other cases one aborted spontaneously; the second had pregnancy terminated at three months by the incision through the anterior uterine wall. A further case is reported where it was supposed that the patient had been sterilized when the interposition operation was performed. Pregnancy, however, occurred, and at three months the patient suffered from inability to empty the urinary bladder. She received treatment for four weeks, when this difficulty disappeared and she went to term. A long, tedious labor, with symptoms of labor for nearly eight days, developed, followed by fever and chills and vomiting, and terminated by craniotomy. A further case is reported in which between the second and third months of pregnancy the uterus, which had been interposed, was separated from its adhesions and brought into its normal position and the pregnancy allowed to continue.

A case is described from the Munich Clinic where a typical interposition operation had been done and both tubes had been doubly ligated with silk. More than a year afterward the patient returned to the hospital, two or three months pregnant. Therapeutic abortion was performed, but no further attempt at that time was made at sterilization. In another case interposition had been practised with excision of a portion of the tubes. In spite of this the patient afterward came to the hospital in a pregnant condition. The vagina had been very greatly drawn up by the development of the uterus, so that the cervix and os uteri could not be felt on examination. The patient was treated by abdominal section, and it was observed that the urinary bladder had also been brought up out of the pelvis into the abdominal cavity. It was over the anterior portion of the uterus, and the peritoneal attachments of the bladder were as high as the fundus. The posterior wall of the uterus was enormously distended, the uterus was opened through the posterior wall and the living child extracted and the tissues closed. Mild infection developed in the abdominal wound, but the tissues made ultimately a good recovery. The uterus returned to its interposed position when involution was complete.

Weber has observed 43 cases, among them 2 deaths. One occurred from biliary tuberculosis, fifty days after operation; the other ten days after operation from diffuse septic infection; 32 of these cases had been treated for total prolapse; the others were operated upon for cystocele and prolapse of the uterus. These patients were all examined after the operation at times varying from six months to twelve years. Three stated that the operation had failed and that prolapse had developed as badly as before the operation. In 20 examined some time after, the results in 15 seemed to be all that could be expected. In 3 there was prolapse in some degree. In general, it might be stated that 97.6 per cent were permanently improved by the operation and 0.4 per cent little or none. These statistics agree in the main with those of other clinics where the operation has been extensively practised.

The Use of Organic Extracts to Stimulate Labor. Köhler⁴² has made experiments with extracts from organs of various warm-blooded animals

⁴² *Monatschrift f. Geburtshülfe*, 1920, vol. vi, No. 52.

to ascertain the effect of these substances on the contraction of unstripped muscle and therefore on the forces of labor. Clinical observation was undertaken in 30 women, 19 of whom were at full term, 7 in premature labor and four times therapeutic abortion was brought about by injecting these extracts. Where the method of treatment brought on uterine contraction the first evidences were seen nine or ten minutes after the first injection, but these contractions were all of short duration and not much intensity. In a few cases these injections were followed by the cessation of labor, which could be made to go on again by a fresh injection. In 4 cases labor had to be terminated by some obstetric operation. When abortion was in progress the use of these injections hastened it. It was interesting to observe that most of these patients complained of a feeling of tension in the breasts after they had been delivered and that there seemed to be distention of the breasts to a more than unusual degree. Apparently, the secretion of milk was greatly stimulated.

In the course of these investigations it seemed to develop that these extracts contain a common substance which holds protein material in combination. The effect produced by the various extracts is apparently identical, and this included also extract from the substance of the placenta. Details are given concerning the method of preparation, and illustrations are added to the article showing tracings obtained when the injections were given.

Anesthesia in Labor. Gauss, in the Fribourg Clinic, contributes a somewhat extensive paper, drawing attention to the value of morphine-scopolamin producing analgesia and anesthesia during labor. He concludes that the entire success or rejection of this method depends upon its influence upon the child. As he puts it: "Obstetric twilight sleep stands or falls with the child. If it can be shown that this method injures the child, then it must be abandoned." In the beginning from 25 to 30 per cent of children showed the effects of overdosing the mother. The condition of these children was often not serious, but still could not be said to be normal. In estimating the results of the treatment, what happens in the first nine days after birth must be taken into account. It must also be determined whether morphine or scopolamine is the injurious substance. Of less importance is the frequency of obstetrical operation in these cases.

The first reports of those using the method show a fetal mortality of 2.1, 2.5 and 2 per cent; others had a fetal mortality as high as 5 or 6 per cent. Beruti and Glock reduced the fetal mortality to 1.1 per cent and 0.89 per cent. Before this method was used in some of these clinics the fetal mortality was between 4 and 5 per cent. In this same clinic the introduction of morphine and scopolamine was followed by a reduction of fetal mortality to 1.7 per cent. It is thought that these substances are carried in the placental circulation of the fetus, and hence a direct effect from their presence must result if they are given in labor.

When the results of this treatment are studied regarding their influence on the mother, it is found that in the Fribourg Clinic amnesia is produced in 99.5 per cent of cases; the frequency of operation becomes

9 per cent. In other clinics the percentage of amnesia reported is much less, while a percentage of weak labor pains from 22 to 50 is also reported. Others report amnesia in 84.9 per cent, with frequency of operation of 7 per cent. In some clinics where the method is used to the extent of lessening the vigor of labor pains the percentage of operation is 16.7 per cent and 15.5 per cent, while in these clinics the use of the forceps was necessary in 14 per cent and 12.3 per cent.

The practical conclusion of this paper is not to reiterate the claims made for the method of producing amnesia but to draw attention to the fact that in the hands of many who have used the method too large doses of morphine have been given. For about a year in the Fribourg Clinic, beginning at a given time, 0.00045 gm. scopolamin with 0.03 gm. narkophin have been given. This dose of scopolamin was repeated in three-quarters of an hour without narkophin. One hour later 0.00021 gm. scopolamin without narkophin was given, and this dose of scopolamin without narkophin was given one hour later and repeated in still one hour. With one dose of an opiate and repeated small doses of scopolamin the writer claims the best results.

The Frequency and Importance of Spontaneous Puerperal Infection. Poten⁴³ reviews the literature of the subject regarding the reports obtained in some of the principal continental clinics. A careful tabulation of the results of the writer's clinic at Hanover shows that a considerable percentage of patients who have no vaginal examinations during labor and no operative or other interference show a rise of temperature during the puerperal period. These patients are never very ill and the elevation of temperature lasts but a short time. Occasionally a case occurs where a fatal issue follows a spontaneous infection. Thus the case of a woman, aged forty-one years, a multipara, is reported who entered the hospital in an apparently normal condition and had a comparatively short and easy labor without interference. Every precaution was taken to maintain asepsis and antisepsis. On the third day occurred a rise of temperature and the patient developed peritonitis and died. At autopsy, there was a small wound in the mucous membrane of the vagina through which infected bacteria had entered. The endometrium had become involved and from thence peritonitis had developed. Attention was called to the practical impossibility of disinfecting the genital tract, and no system of douching or the application of antiseptics will entirely destroy bacteria in the vagina.

The Mortality of the Newborn Arising in Labor. Schott⁴⁴ has made a careful study of the various complications which may injure the child during birth. This is especially true of cases in which some mental or physical condition or some abnormality of the nervous system, like idiocy or epilepsy, has developed.

As regards idiocy and lack of mental development, injury in birth could be traced as the only cause in 2.81 per cent; difficult labor alone, without inheritance or without other complications, was followed by mental or nervous abnormality in 3.63 per cent; the use of forceps alone

⁴³ Archives f. Gynäkologie, 1920, ii, No. 113, 316.

⁴⁴ Ibid., 336.

in 0.54 per cent; premature birth in 0.45 per cent, while there is a very considerable injury to the nervous system in those cases born apparently asphyxiated. This sometimes results from pressure on the umbilical cord, sometimes from pressure on the child's brain, premature birth before twenty-eight weeks and also the bleeding of a hematoma or blood tumor over the cranium. Premature birth may also occur through some very serious condition of the mother, as disease of the heart or lungs, hemorrhage or separation of the placenta. The mortality of children under these conditions frequently rises to 30 per cent. It is very difficult in such cases to estimate just what influence the temporary condition of asphyxia in the child has had in producing permanent results in the nervous system, but if asphyxia alone be considered it is undoubtedly a cause in 2.44 per cent of cases of deficient development of the nervous system. Twin birth is productive of nervous complications in the children in 0.18 per cent, and the same percentage arises in cases in which the child is born suddenly and sometimes with very strong pain. In the birth of triplets, permanent injury to the nervous system resulted in 0.09 per cent. Hemorrhage from the umbilicus could not be recognized as the only cause of abnormality of the nervous system in any case, but was a general cause of morbidity in 0.09 per cent. Asphyxia and convulsions, alcoholism in the parents and near relationship of parents are important factors in producing disease of the nervous system in the newborn. It is interesting to observe among cases of idiocy that six times as many could be traced to a long, tedious labor as to those cases in which birth was terminated by the prompt use of forceps. There is, however, a distinct relationship between idiocy, epilepsy and difficult birth. Intracranial bleeding is a reason of special significance in the newborn from whatever cause it may have arisen, and this usually occurs near the vault of the cranium, over one or both hemispheres. Less often bleeding is at the base of the brain or at the cerebellum. Laceration of the tentorium is also a not infrequent result of complicated labor.

Regarding epilepsy developing after difficult birth and complicated labor, it may be taken as a cause in 1.9 per cent of cases; the uses of the forceps alone in 0.09 per cent; difficult birth alone in 0.27 per cent; asphyxia alone in the same percentage; premature birth in 1 per cent; twin birth in 0.9 per cent; hemorrhage from the umbilicus in 0.09 per cent.

In reviewing the literature, it is found that while epilepsy is comparatively frequent, and more frequent than idiocy and permanent impairment of the nervous system, difficult labor is not a direct cause of epilepsy so frequently as might be expected. If the percentage of cases in which permanent impairment of the nervous system, resulting in impairment of the mind, be taken it may be placed at 2.81 per cent; where difficult or complicated labor occurred, in cases of epilepsy and complicated birth, it was not present in more than 0.09 per cent. If cases are taken where there was not only difficulty in labor but bad inheritance, parental drunkenness, parental disease and all possible complications affecting the newborn, then permanent injury to the

nervous system resulted in the newborn in 13.63 per cent, while in the same cases epilepsy developed in 8.54 per cent.

Intravenous Use of Drugs to Produce Amnesia in Labor. Eisenberg⁴⁵ calls attention to the use of what is termed "amnesin," a preparation of quinine and narkophin with scopolamin, by intravenous injection, to produce amnesia during labor. This solution is prepared by treating a quinine salt with lactic acid, thus producing a less acid combination than when the cinchona base is treated by stronger acids. The scopolamin solution is also prepared by concentrating it, and both solutions are adapted to the condition of osmosis normally pertaining in the blood serum. The combination of the quinine preparation with a derivative of morphine called "narkophin" was called "amnesin," and of this solution 1 c c was combined with 0.0003 gm. scopolamin. The cubital vein was selected for injection, and three or four injections were necessary during a labor. The last one was given as soon as the presenting part became visible. A prompt and successful action of the remedies was secured by this method.

Siegel is convinced that the lessening of the quantity of morphine in the modern scopolamin-morphine treatment is of very great importance. He quotes the statistics of several clinics having large material, and the figures given would indicate that what is termed the "simplified" method gives better results for both mother and child. This method consists in giving but one dose of morphine with the quinine derivative, accompanied by a minute dose of scopolamin. Scopolamin is then given in repeated but small doses as long as its effect is desired.

OBSTETRIC SURGERY.

Cervical Cesarean Section. Lichtenstein⁴⁶ contributes an extensive paper, on this subject from the Zweifel Clinic in Leipsic. In beginning his paper, he remarks that it is more difficult than ever to give a sharply-defined position to Cesarean section. He alludes to the different varieties and then describes his results in 143 cervical Cesarean sections.

Non-complicated contracted pelvis was the occasion of operation in 107; contracted pelvis with complications in 20; normal pelvis with ovarian tumor in 2; eclampsia in 6; placenta previa in 7; neurofibroma molluscum in 1.

In the first 48 cases he made a transverse incision through the abdominal wall and in the last 95 cases he made a longitudinal incision through the abdominal wall; in all the operations the cervix was opened longitudinally.

The peritoneum was entered in five different ways; none of these was new and all have been described and practised by other operators. He recognizes the fact that many operations result in wounding the peritoneum no matter what method be employed. In 3 cases the peritoneum of the abdominal wall and that of the viscera was closed by suture, so that the peritoneal cavity was not open; after the operation the visceral

⁴⁵ Zentralblatt f. Gynäkologie, 1920, No. 26, p. 688.

⁴⁶ Archives f. Gynäkologie, 1920, No. 112, p. 15.

peritoneum was used to cover the line of suture. In 1 case where the child was extracted by breech presentation the visceral peritoneum was torn in two places. In 11 cases the parietal peritoneum was opened above the bladder, and under direct vision the visceral peritoneum was separated from the bladder and cervix and drawn up as high as possible. When this was accomplished without wounding the peritoneum the operation was performed and the tissues closed after the operation. In 4 cases the peritoneum was opened and in 2 there were several points of laceration. In 2 cases the urinary bladder was wounded, the only time that the accident occurred in all the operations. This wound healed by first-intention and apparently did no harm, and one of these cases was afterward delivered by Cesarean section. In 11 cases Latsko's method was followed, and after mapping out the position of the child the bladder was drawn up on either the left or right side, usually on the left, and filled with 250 cc of water. In 5 cases the cervix was freed without wounding the peritoneum; in 6 the peritoneum was torn, but there was still sufficient space to permit carrying out the operation; in 3 of the cases the operator was obliged to make his second operation intraperitoneal. On one occasion, when the effort was made to push the serous tissue as far up as possible, varicose veins within the peritoneum were ruptured and profuse hemorrhage followed. In another case the bladder could not be pushed up on the left side, and when the effort was made on the right side the peritoneum was torn. In another case there were adhesions following a pelvo-peritonitis after previous confinement, which made it practically impossible to separate the visceral and parietal peritoneum.

Twelve cases were operated upon by what the writer terms the method of Latsco-Zwiefel. In this operation the bladder is pushed so far away from the site of operation that the cervix can be incised in the median line. This avoids unusual hemorrhage. In the operation known as Latsco-Doederlein-Kustner the peritoneum is pushed up without completely separating it from the bladder. If the median vascular ligament is exposed, this is severed, which permits the easy separation of the bladder and cervix so that the cervix is easily opened in the median line. This procedure was easily carried out in these cases; in 1 case, however, there was a tear of the peritoneum, and in 2 cases there were severe lacerations. These were closed and the operation carried out practically as an extraperitoneal. One hundred and six cases are described as intraperitoneal; among them are 3 with the Latsco method followed and the remaining 103 were primarily intraperitoneal operations. In some, the operation was performed as rapidly as possible in the interest of the child; the parietal peritoneum was excised longitudinally; the empty urinary bladder was pushed backward; the visceral peritoneum was not separated, but the anterior portion of the upper extremity of the wound in the abdominal wall was covered with a sterile towel and then the cervix opened through its entire wall. The cervix was closed by interrupted sutures and the peritoneum by continuous sutures. If labor had been long and the cervix was not completely dilated, the upper portion of the cervical wound would frequently tear into the lower portion of the expulsive segment and the lower uterine segment. Drainage

through the abdominal wall was employed in no case and a drainage tube was passed through the wound in the cervix through the vagina; this patient had a temperature of 104° during the labor. In ascertaining the frequency of peritoneal injury in 33 operations, the peritoneum was unintentionally opened in 15; in 23 performed by a slightly different method the peritoneum was opened in 12.

From his experience the writer concludes that injuries to the peritoneum is less frequent the longer the patient has been in labor with good pains and the more completely the cervix is dilated. When this operation was first recommended, the operator was advised to wait in labor as long as possible, because the peritoneum would separate more easily from the surrounding tissues than during the first stage of labor. This is found to be only true when the fetal membranes have not been ruptured. If the membranes rupture early in labor, as they often do in contracted pelvis, the os uteri may remain practically unopened and the cervix does not retract. In these cases it is very difficult to carry out operation in the extraperitoneal way. One must not forget the danger of infection, which increases with the length of labor. This led the writer not to wait for a long labor before performing the operation even if the peritoneum is not open and the serosa is very greatly thinned in the process of pushing up the tissues; if the serosa is closely examined with a bright light numerous small openings can be demonstrated in it. There is also danger of necrosis if the tissues have been very greatly thinned; such cases do worse than if the normal peritoneum is opened by a small tear and the injury immediately repaired. The thinned portions of the tissues can be seen especially clearly and an aseptic fluid is found in the pouch between the bladder and the uterus. In repeated operations, adhesions are often found in this region, which shows that injury to the peritoneum had occurred in the first operation. These conditions are of importance when the effort is made to deliver patients before treated by cervical section. At the time of difficult labor, when operation is indicated, it is difficult to demonstrate positively the presence of infection; there is no time to make bacterial cultures, and even the presence of streptococci in the cervical secretions is not proof positive for such may not be pathogenic. There is a form of streptococcus found in lactic acid secretion which are not pathogenic. Even the presence of hemolysis is not a positive proof. It has been urged that material taken from the tissues be used to inoculate animals and that the result would enable one to form a diagnosis concerning the puerperal period. While this may occasionally be possible it would be an exception, and one must admit that we have no method of positively estimating the resistance of the tissues to organisms and the development of infection. We must fall back upon clinical symptoms, and stress may be laid upon the labor, long-continued, after rupture of the membranes, examinations made outside the clinic by physicians or midwives and fruitless attempts at delivery. Experience, however, has shown that even when the membranes have been ruptured for some time and there is slight elevation of temperature that the cervical section may still give good results. One must not forget that fever during and after labor

may arise from causes outside of the genital tract; thus in one case of eclampsia pneumonia developed with fatal results. Another patient had double ovarian tumors of a malignant nature with some elevation of temperature, and on the third day after Cesarean section the abdomen was reopened for obstruction of the pelvis and the patient recovered, and was discharged on the twenty-fourth day after the first operation with both wounds perfectly healed.

One patient had high temperature and the membranes had ruptured seventeen hours before the operation; drainage was used, but the high temperature persisted for twenty-five days. The transverse incision suppurated and thrombosis developed; this patient recovered after forty-six days' illness. In another case the amniotic liquid had escaped thirty-eight hours before operation and the peritoneum was wounded during delivery. The peritoneum healed after the operation, but the transverse abdominal incision suppurated and the patient had fever for fourteen days. Her recovery consumed in all forty-eight days. The third case had central placenta previa with unruptured membranes; she had been tamponed before admission and had a temperature of 102.5° . She was severely anemic and had a hemorrhage. Intraperitoneal section was done, the patient dying on the sixth day from septic thrombosis and embolism.

In 129 Cesarean sections there were 2 deaths, 1.4 per cent. The results of intraperitoneal operation were no worse than those of extraperitoneal. In 94 intraperitoneal operations there was 1 death, with a mortality of 1.6 per cent. In 35 extraperitoneal operations the mortality was 2.8 per cent. The results with eclampsia and placenta previa are usually worse than when these complications are not present. In 143 Cesarean sections there were 8 deaths with a mortality of 5.6 per cent; in the extraperitoneal cases mortality was 8.1 per cent and in intraperitoneal cases the mortality was 4.7 per cent.

The writer then analyzes the fatal cases in the intraperitoneal sections: One had a highly contracted pelvis and had been examined by a midwife and a doctor. One had a shoulder presentation and was delivered of a living child which survived; this patient had had an injury to the bladder previously which had been ruptured, and after a Cesarean operation she had incontinence of urine. On the fifth day she died from peritonitis, and section showed a permanent fistula between the vagina and the bladder, with septic ureteritis and pyelitis and endometritis and peritonitis. One eclampsia patient died of pneumonia through inspiration during her convulsions, as proved by autopsy. The second was eclamptic and severely asphyxiated, recovered from eclampsia, had suppuration in the abdominal wall and developed a phlegmonous inflammation of the pelvic tissues which caused a fatal peritonitis. Another patient had neurofibroma molluscum, the gluteal peritoneal regions being covered by these tumors. The external genitalia were greatly inflamed and the vagina admitted two fingers with difficulty. A living child was born by section, but a very severe hemorrhage developed from the uterine incision; this could not be controlled and the patient died from hemorrhage. At autopsy, the recto-vaginal septum

was $5\frac{1}{2}$ cm. thick and the tissues about the bladder were extensively involved. Another patient had placenta previa, had been tamponed before admission and was brought in bleeding and in collapse. A bag was immediately inserted, the fetal membranes were unruptured and an incision through the cervix was extended through the placenta. The child was stillborn and could not be revived. The patient developed peritonitis, with thrombosis, and died on the sixth day. At autopsy, it was shown that the stitches through the cervix and serosa did not hold and that the peritoneum for this reason readily became infected.

The writer considers that these cases do not in any way militate against the intraperitoneal operation.

He then analyzes the deaths from extraperitoneal section. The first was an eclamptic brought from her home unconscious without previous history. The fetal membranes were unbroken; the temperature was 104° . The child was born living and died on the second day in eclamptic convulsions, and an autopsy showed characteristic lesions in the liver. The mother had fifteen convulsions after operation, a high fever and developed pneumonia. Autopsy showed gangrene and abscess of the lung with empyema.

A second eclamptic patient, admitted with ruptured membranes, had eight convulsions before the operation, and during operation a considerable tear was made in the peritoneum, which was immediately closed. The child was delivered by forceps, living, and the patient's convulsions ceased. She had high fever, and on the fourth day the abdominal wound was reopened and a large cavity found under the fascia filled with pus and swarming with streptococci; death occurred the next day and an autopsy showed an open rent in the peritoneum with a large abscess. This patient's viscera showed no signs of alteration from her eclamptic condition. In one fatal case after extraperitoneal section the patient had highly contracted pelvis and had previously given birth to three dead children. The membranes were unruptured and a bag was used to complete dilatation and an effort made to close the two layers of peritoneum by suture before the operation. After the delivery of a living child, which survived, it was found that these tears had opened during delivery. The patient was restless after operation, with a high fever and a foul lochia. A thin secretion escaped from the wound, which was reopened through its entire extent and disinfected with hydrogen peroxide, and a wet dressing applied. Streptococci were found in the wound and on the fourth day death occurred. At autopsy, there was a phlegmonous inflammation through the connective tissues to the pelvis in the vicinity of the bladder; pus was present and there were three openings in the peritoneum connecting with the cervix. The stitches in the cervix held. The patient died from septic endometritis and the spleen showed evidence of infection. It seemed fair to charge these two fatal results to the operation, because inflammation occurred from wounds and injury made during the operation.

An interesting case reported by Pankow is stated in which on the eleventh day after operation, where fever had occurred and subsided, the patient had a rapid rise of temperature and died on the fifteenth day.

On section, a large retroperitoneal abscess had formed into which pus had entered from the abdominal cavity. In this operation a coarse drain had been used, fearing the development of infection.

The writer cites the reports of others and alludes again to his two fatal cases, after extraperitoneal operation, which were lost through infection of the connective tissue in the wound. The writer does not believe that the intra- and extraperitoneal operations can be fairly compared. When an incision is made through the body of the uterus it often passes through the placental site, and this may readily become infected and bring about a fatal issue. With the exception of the placenta previa this is not the case where cervical operation is practised. In the cervical operation the line of union is not subjected to the tension and disturbance occurring in an operation through the body of the uterus; furthermore, the cervical wound is readily covered with the serosa, and this tends to prevent the entrance of material from the uterus into the abdominal cavity. For this reason the writer inclines to the belief that incision through the body of the uterus would probably be abandoned for that through the cervix. He considers, however, the intraperitoneal operation is safer because it avoids injuries and lacerations in the vicinity of the bladder; this occurs in the extraperitoneal method, and even if a fatal issue does not follow the patient may be left with permanent injury to the bladder, the results of which are most distressing. It must not be forgotten in cases where active infection is evidently present; it may be safest to perform a Porro operation or to perforate even the living child. It is always difficult to decide positively on what grounds one would perform the intraperitoneal section or operation through opening the pelvis.

The fatal mortality in 143 Cesarean sections was 9.63 per cent. Three of these children died in cases of contracted pelvis, 3 in eclampsia, 2 in placenta previa and 1 in angiosarcoma of the ovary. In 106 intraperitoneal operations there were 5 fetal deaths, 4.7 per cent; and in 37 extraperitoneal sections there were 4 fetal deaths, 10.8 per cent. In 16 cases of intraperitoneal operations, sterilization was practised.

Including his own cases, the writer has collected the maternal results in 1000 cases of Cesarean section with a mortality of 3.9 per cent, which is rather high, but it includes cases of eclampsia and placenta previa. Of these operations, 532 were intraperitoneal with a maternal mortality of 3.6 per cent; 468 were extraperitoneal with a mortality of 4.3 per cent. Undoubtedly, the fetal mortality of extraperitoneal operations must be greater than that of intraperitoneal operations. The writer further considers the question of cervical section in transverse presentation. Here he believes intraperitoneal operation is the best; if there is any injury occurring to the surrounding tissues they can readily be seen and immediately repaired.

It is interesting to note the condition of the scar in the uterus in subsequent pregnancies and labor and also what may be the condition of these women when not in the pregnant state. The question as to whether the cervical scar is more liable to rupture in subsequent pregnancy than the scar through other portion of the uterus is of great importance. Schauta found the scar after cervical section to be but 1 mm. thick.

This observation has been repeated by others. In one instance the patient had two cervical sections, one on the right and one on the left side of the cervix, and on microscopic examination these scars showed no thinning. The portion of the tissues through which the stitches had passed had filled with epithelia, and such a process occurring in the cervix must predispose to rupture. This epithelial growth had occurred because the catgut stitches had been taken in the mucous membrane of the cervix and epithelial cells had grown in the stitch canal. Evidently the mucous membrane of the cervix is better avoided in making closure. Other writers, in repeating cervical section, have found great thinning in the cervical scar. In one of Bumm's cases the scar was so thin as to resemble the urinary bladder; this patient had had two cervical sections previously. One cannot then say that by cervical operation the danger of rupture of the scar is entirely avoided; ruptures are reported, one of which occurred transversely in the upper portion of the cervix and the longitudinal scar held. Another patient had an intra-peritoneal cervical section followed by rupture of the scar in a following pregnancy. Close examination of the specimen showed, however, that rupture had occurred in the lower portion of the body of the uterus and could not be justly charged to the cervical operation. When an intra-peritoneal operation rupture occurred, because at the operation the opening in the cervix was too small and tissues had not torn at the site, this did not demonstrate the fact that the cervical scar was weak. Another patient had cervical section in lateral placenta previa; the cervix was opened in the median line. In a following pregnancy the physician endeavored to induce labor at the ninth month; a laminaria tent was introduced, pains developed and after twelve hours the membranes ruptured. The patient suffered severely and was given morphine; on the next morning uterine contractions and pains ceased, the child was dead and the cervix was fully dilated; the patient was sent to the clinic and on section there was a long tear on the left side of the cervix through which the child had escaped into the abdominal cavity. The patient was treated by supravaginal hysterectomy, with recovery after suffering thrombosis. This case the writer considers rupture after cervical section, but not as a consequence of cervical section. Microscopic examination of the intact scar showed no growth of epithelia in the stitch canals.

Thirty-four patients had become pregnant after delivery by cervical Cesarean section; 25 of these had repeated section, 1 had supravaginal amputation, in 2 craniotomy was done outside the clinic, 3 had abortion outside the clinic, 1 premature labor between the eighth and ninth months, and in 2 the writer was called in consultation to make the diagnosis of pregnancy, one at the eighth and the other at the fourth month. Six patients had two pregnancies after the first Cesarean section, in 1 of which the physician brought on labor and emptied the uterus twice at the second month; another aborted twice in the third month; 1 gave birth spontaneously to a full-term child and in the next pregnancy was again delivered by intra-peritoneal section. In 3 patients the intra-peritoneal section was repeated in 2 and in 1 case extensive adhesions

were found in the vesico-uterine pouch. As a rule the scar in the cervix was not visible during this operation and there was no evidence of thinning of the scar. None of these 34 patients suffered from disability during pregnancy occurring after cervical section which could be referred to the scar; even those cases delivered outside the clinic after operation seemed to have had no special difficulty. The writer believes, from his experience, that the scar is a sound one and that it will endure the strain of subsequent pregnancies. He had examined 29 patients to determine their ultimate condition after cervical section; none of these was pregnant. In none could he find evidence of the scar or hernia in any portion of the tissues. Some had hernia as a result of drainage. In 7 of the 29 cases there was retroflexion of the uterus and 3 of these had intraperitoneal section. The uterus could readily be found on examination, was anteflexed in 19 and in 1 case was completely retroverted; here the uterus was drawn transversely, the cervix toward the left the fundus toward the right. It could not be brought in the median line; this patient had one section by the extraperitoneal method and later one by the intraperitoneal method. Nineteen of these women complained of nothing as the result of the operation; 1 had developed fibroma of the abdominal wall which was painful, and this fibroma was removed, giving the patient relief. Five complained of pain in the abdomen, 4 on the left side and 1 in the sacral region. These 5 patients could not localize distress at any one point. In the 4 patients who had complained of pain on the left side the cervical incision had been made on the left side in 3 and in 1 on the right; this last patient had a retroflexed uterus and the others anteflexed. Three women complained of irregular menstruation and 3 of difficulty in emptying the bladder; 1 of these was obliged to empty the bladder frequently; none of these patients had a serious disability.

The writer had 7 cases of placenta previa, of which 6 were delivered by cervical section, and he considers the previous use of the tampon to be a complication of such importance as to forbid the classical Cesarean operation. He is conservative in his views on section for this condition, and in cases admitted in good condition without much hemorrhage he would try absolute rest in bed in the hope of prolonging pregnancy to spontaneous labor. In placenta previa, hemorrhage is an important element, and any method of operation must be judged in accordance to its tendency to increase or diminish hemorrhage. In his 7 cases there was 1 death, the patient who had been tamponed by the physician and examined by a midwife before admission.

In summing up his experience of cervical section, the writer is not prepared to admit that infected cases will always give the best results by cervical section. In some cases the results would be good and in others serious, with high mortality; this will occur whether the operation is extra- or intraperitoneal. The writer does not believe that the extraperitoneal method gives better results than the intraperitoneal method. The danger of infection in the connective tissue is a very considerable one. An effort should be made to reduce the maternal mortality, as most of these patients are comparatively young and may bear children

later. He believes that patients having high fever should not be delivered by extraperitoneal section. The operation can be done more quickly and simply by the intraperitoneal method. The indications for section through the body of the uterus he believes should be considerably enlarged. He would not hesitate to operate on patients whose fever is not above 102° , although patients have been examined outside the clinic and in whom membranes had been ruptured for some time. He believes, however, that incision through the body of the uterus is less valuable than through the cervix. There is not, in his view, great danger of rupture of the cervical scar, but it cannot be doubted that such rupture occurs and that it may occur. The condition of these patients after operation and when not pregnant is in the main satisfactory. Dislocation of the uterus is comparatively rare and complications arising from the bladder are not frequent. The results of extraperitoneal section in this regard are not so good as intraperitoneal. In placenta previa the danger of hemorrhage is not so great as has been stated. Hemorrhage, however, may readily occur, and the operation is to be strongly recommended in comparison with the use of dilating bags and version.

The writer further considers perforation of the living child before and after cervical Cesarean section. He finds that the hope that cervical section would do away with perforation has not been realized. He recognized the high fetal mortality of induced labor. He draws attention to the fact that many children in cases of contracted pelvis become injured from birth and that it is impossible for them to survive even if alive when born. Under these conditions it is justifiable to perforate a child to avoid unduly wounding the mother. In comparing the results of clinical work before and after the introduction of cervical section, he finds that the number of perforations in the clinic have been reduced to one-fifth the previous number by cervical Cesarean section. The percentage of perforation before the operation was adopted was 0.75, after the operation 0.18.

He analyzed by statistics the indication for perforation before the operation and those after the operation, showing that after the operation was introduced perforation was limited to cases complicated by severe and practically fatal conditions.

Cesarean Section. This interesting and important subject has called forth several important papers, and one of special value. Before the Section of Obstetrics and Gynecology of the Royal Society of Medicine a discussion was held on the rupture of the Cesarean section scar in subsequent pregnancy or labor. This valuable material is reported in full in the *Proceedings of the Royal Society of Medicine*, November, 1920, vol. xiv, No. 1, Holland contributed an extended paper in which he gives an account of five cases of rupture of the scar after Cesarean section not previously reported. He also adds an analysis of the literature, the discussion of the etiology and anatomy of ruptured scars and an abstract of the cases hitherto reported. He has tried to trace the history of the large number of Cesarean section patients operated on by English obstetricians between 1912 and 1918 inclusive.

Three of the new cases reported have nothing of unusual interest except the fact that a Cesarean section had been performed and that the uterine wound had been closed with chromicized catgut. Rupture occurred when a subsequent labor developed. The fourth case had her fourth pregnancy terminated by section, the uterus closed with chromic acid catgut, with a temperature 103° on several occasions during convalescence. The fifth pregnancy terminated successfully by the use of forceps, although there was again elevation of temperature. In the sixth pregnancy the patient, while sitting, was suddenly seized with intense abdominal pain. On admission to the hospital and section, the scar on the anterior surface of the uterus had almost completely ruptured; there had been a complete failure of muscular union. This rupture was rapidly closed with interrupted sutures of silk, and the patient made a good recovery. The fifth case had section done under spinal anesthesia for eclampsia. The uterus was closed with silk and catgut and there was some elevation of temperature during the puerperal period. During the next pregnancy the patient had a premature confinement outside the hospital, followed by puerperal sepsis. The placenta was retained and was removed manually two hours after the birth of the child. On admission to the hospital the patient was very ill, with high fever, rigid, tender abdomen, blood cultures negative and perineum completely torn into the rectum. The patient lived for two weeks, having a foul discharge which became fecal.

At autopsy, there was general purulent peritonitis, adhesions between the uterus and surrounding organs, perforation in the wall of the intestine and perforation in the anterior wall of the fundus of the uterus. There were foci of pus in the tubes. The uterine scar had ruptured in its lower two-thirds and there had been a utero-intestinal fistula. It is probable that the intestine was injured when the scar ruptured spontaneously during labor and that the perforation subsequently developed. The retention of the placenta was probably due to its partial escape into the peritoneal cavity.

The writer has found accounts of 92 cases which he has abstracted.

When the scar is studied it is found that in rupture muscular tissue did not develop as normally as it should in the scar. In cases of extreme thinning the attenuated scar consists of peritoneum in contact with decidua, with a few intervening strands of fibrous tissue. The uterine muscle in these cases has completely failed to unite; the sutures employed to close the incision slough out or are cut out; the muscle surfaces retracting become widely separated. The peritoneum holds and the retracted muscle becomes smooth and rounded and covered by a layer of endometrium, which in a subsequent pregnancy is converted into decidua. The appearance of such a rupture is as if the whole thickness of the uterine wall had been newly torn through, whereas in reality it is only the stretched deciduo-peritoneal area which has given way.

Unknotting of the sutures after Cesarean section has been observed both in cases in which catgut was used to close the uterus and less frequently where silk had been employed. Where the tissues open but

partly the scar may be quickly sealed or plugged by omentum, and this would act as a protection.

Utero-abdominal fistula is not very uncommon and is not a serious accident for the mother unless the tissues rupture and the uterus opens into the abdomen.

The site of the incision is of interest, and, theoretically, transverse fundal scars are especially likely to rupture. In this incision the muscle bundles are cut at right angles and imperfect union may result, and, furthermore, the fundus is the part of the uterus relatively most distended during pregnancy, and hence a scar in this part of the uterus will be more distended than in some other portion. It is too soon to obtain an accurate idea of the results in the more recent transperitoneal or extra-peritoneal cervical operations. So far as reports go, fewer ruptures have occurred after this operation than after others. Cases in which the cervical scar has been found greatly thinned have been reported.

In vaginal Cesarean section very few reports are available as to the subsequent behavior of the scar.

The influence of the situation of the placenta over the scar is a point of importance. In 51 in the 97 cases this fact was ascertained; in 34 it was over the scar; in 17 it was not. While this would indicate that the situation of the placenta predisposes to rupture the inference is not a strictly fair one, for in cases of repeated Cesarean section the placenta has often been found over the scar without a harmful effect. There is no histological evidence to show that chorionic villi invade scar tissue more than they invade normal uterine tissue. The examination of uteri removed after Cesarean section and found perfectly healed indicates that the implantation of the placenta is not an important factor. When, however, retroplacental hemorrhage occurs this may be a factor of importance in determining the healing of the scar.

The study of reported cases shows clearly that of all causes for imperfect healing of the scar, sepsis is the most important. In the writer's collection of cases, in 51 there was fever or definite uterine or abdominal sepsis. In only 15 of the 66 was there a recovery without fever. If the septic process be severe, uterine tissues will undergo necrosis, sutures will cut out, muscular walls will retract and scar will form, consisting of little more than peritoneum, with a protective layer of omentum or other adhesions. Even if the sutures do not cut out the wound will granulate and form a broad fibrous scar. If silk has been used, suppuration will continue until the silk comes away, sometimes in the uterine discharges. Attention is called to the fact that infection of a uterine wound may occur without rise of temperature or with so slight a disturbance that sepsis is not suspected. The presence of extensive adhesions to the scar at a subsequent operation is evidence of sepsis during healing. The writer believes that Cesarean section can never be guaranteed as a surgically clean operation. There is a large wound in a mucous cavity in direct communication with or within a short distance of a contaminated area. In 84 cases of section recovery was afebrile in only 38, or 45 per cent.

In the management of future pregnancies it is of the utmost import-

ance to study the type of convalescence from a Cesarean section. If there has been fever and other evidence of sepsis, or if convalescence has been without fever, the chance of fever is a very small one, but there can be no absolute guarantee against rupture, because infection may not have been detected.

Suture material and method of suture are most important. Catgut has serious disadvantages, because of its sometimes rapid absorption and the fact that it readily becomes infected. In the non-absorbable sutures silk or linen thread and silkworm-gut are proposed. While, theoretically, silkworm-gut is better, it is sometimes difficult of application, because it is so little flexible. No case has been reported in which rupture of the scar has occurred where silkworm-gut had been employed. It is also of great importance in suturing that the operator waits until complete retraction has occurred. If the wound is sutured before retraction is complete and the muscular walls are thin, the scar is bound to be thinner than the rest of the uterine wall.

It cannot be denied that there are accidental factors of importance in producing rupture of the uterine scar. Overdistention of the uterus in pregnancy by hydramnios, excessive size of the fetus, twin pregnancy, a large retroplacental hemorrhage, the introduction of a hydrostatic bag, prolonged or obstructed labor, internal version and the use of pituitrin are all important. In one case reported the patient fell out of bed and the uterus ruptured from the shock and violence done to the abdomen during the fall.

Experience shows that patients who have had Cesarean section may deliver themselves safely in a subsequent pregnancy, only in a later gestation to have rupture occur. Ordinarily this accident happens at full term or within a month of it, and during labor in 48 and before the onset of labor in 36. The first stage of labor is usually the period of parturition where rupture occurs. Unfortunately, rupture of the Cesarean scar may occur during pregnancy from the seventh month on. This renders the critical care of the Cesarean patient more difficult.

While we are familiar with the usual signs and symptoms of ruptured uterus this accident may be followed by very slight symptoms if the rupture of the scar is gradual. Where one point yields a small bag of membrane bulges through and the patient may go into labor with complete rupture of the scar developing very gradually. The severity of the symptoms is largely dependent on the position of the placenta. If this is over the scar, hemorrhage is likely to be very severe. If the placenta is well away from the scar, the placenta separates and is expelled into the peritoneal cavity with very little more hemorrhage than occurs after a normal third stage of labor. Where the rupture is partial and the ovum is still in the uterus, obviously acute symptoms will not develop. Symptoms are sometimes completely absent or may be slight and misleading. A case is even reported where there was no intra-peritoneal hemorrhage or shock. There was profuse abdominal pain for a few days, after which the patient was comparatively comfortable and walked about with little inconvenience.

The writer believes that it is impossible, from existing literature, to

determine the frequency of rupture of the Cesarean scar. This was his object in endeavoring to follow cases operated upon between 1912 and 1918.

The writer finally collected the obstetrical history of 1103 cases of Cesarean section, from which he draws his conclusions. From this he finds that the true frequency of rupture is 4 per cent. There is 1 case of ruptured scar to 4.3 successful deliveries by the natural passages. He further endeavored to ascertain what sort of material was employed in closing the uterus, and he finds that in cases in which the uterus was closed with catgut there was 5 per cent of rupture while in cases closed by silk there was 2 per cent.

Munro Kerr believed that in conservative Cesarean section the uterine scar is frequently unsatisfactory. In his personal experience he has found there is a relative sterility following Cesarean section of 42.6 per cent, that abortion is relatively uncommon in 5.3 per cent, that liability to rupture is present in 5.5 per cent, and that rupture actually did occur in 1.8 per cent. He states that the uterine scar is frequently defective because it is difficult to secure complete asepsis in operating upon the uterus. During the puerperal period the uterine muscle undergoes degeneration by autolysis. This is unfavorable for union. The sheets of muscle which form the uterine wall are irregularly distributed, and hence the wound can never be in absolutely smooth approximation. The uterus contracts after the operation, and this tends to separate the tissues. The surgeon must use his stitches not only to bring together the tissues but to check bleeding from the uterine sinuses, hence the stitches are drawn tightly, which in some cases may interfere with a smooth healing. Furthermore, in many cases the placenta is under the incision, in 40 per cent as estimated, and this renders still more difficult the accurate approximation of the wound.

Kerr urges that every precaution be taken to prevent infection. Wherever possible he would force the placenta through the cervix and have it delivered through the vagina. This can be done in cases in which the cervix is largely dilated, as in contracted pelvis; but when section must be done in emergencies like eclampsia and separation of the placenta it would be impossible to deliver the placenta through the unopened cervix. The wound in the uterus should be closed in layers and silk should be employed to bring together the muscular tissue. The uterus should be sutured while it is in a state of retraction in distinction to contraction. This condition is usually present in the ten or fifteen minutes immediately following the delivery of the child.

The writer believes that a scar through the lower uterine segment will stand a subsequent pregnancy better than the scar of a classical Cesarean section. He has operated with this end in view by having the patient prepared in the ordinary way, the vulva, vagina and cervix being carefully disinfected. A longitudinal incision is made, reaching from below the umbilicus as far as the symphysis. After the abdomen is opened, the bladder is dissected off from the anterior uterine wall. A large retractor is inserted in the lower part of the abdominal wound to bring the lower segment within easy access. The transverse incision is

made in the lower segment and a suture is inserted in each end of the wound, serving to control any laceration at the ends of the wound and after delivery to pull up the wound, so that it can be easily stitched. The extraction of the child is accomplished sometimes with the hand, sometimes with one blade of the forceps used as a vectis, and in other cases the two blades of the forceps are used. When the child has been delivered and the cord tied, the placenta may be removed through the wound if the cervix is not sufficiently dilated; but if the cervix is dilated, the cord is dropped into the uterine cavity and the placenta is delivered through the vagina. The wound is pulled up so that it is easily accessible for stitching and three layers of suture are inserted; catgut in the mucous membrane, linen thread in the muscle and a third layer of catgut, which restores the bladder to its old position. By experience the operation has been found not difficult. It is not extraperitoneal nor is it claimed to be, but it is believed that the cicatrix will be less liable to rupture. In making this incision there is usually very little bleeding unless the wound extends to the vessels at the side, which happened in one of the early cases. The wound is readily closed, and in one case where a strip of tissue was removed it was found that the transverse fibers were more numerous than the longitudinal ones. It is thought to be a very great advantage that after this operation the wound area is at rest during the early days of the puerperal period. The incision is usually remote from the placenta, and it is also believed that the scar is in a safer region than in the ordinary case. The writer had 2 cases of spontaneous delivery after this operation; in 2 others Cesarean section was employed for the second time; in 1 spontaneous case the hand was introduced into the uterus and the lower segment carefully examined. There was no trace of a wound or of thinning of the segment.

Barris had followed up 48 cases of Cesarean section which had been done at St. Bartholomew's Hospital. No rupture of the scar had occurred. In these cases the wound was closed by interrupted silkworm-gut sutures passed through the muscle only. Unfortunately the silkworm-gut sutures are practically permanent, and in 1 case a patient returned suffering from metrorrhagia, and on dilating the cervix several silkworm-gut sutures were removed from the inner wall of the uterus. In his cases 58 per cent subsequently became pregnant. He believed that in clean cases the classical Cesarean section at present is the best operation, provided the patient is not to be sterilized. Catgut should not be used in the muscle, and if infection occurs it greatly increases the risk of rupture of the scar.

Amand Routh had collected 1282 cases of Cesarean section in 1910, with a mortality in contracted pelvis in clean cases under 3 per cent. Fear of rupture of the scar led to the performance of sterilization in many of the early cases, but in 1910 the percentage of cases not sterilized had risen to 89. In 112 patients who became pregnant after section, 3 seemed to have had a rupture of the scar, but this is not an absolutely accurate study of these cases. To secure perfect union he would make the incision in such a manner as to avoid, if possible, the placenta. The transverse fundal incision is not advisable as the operation should

be done at full term or at the earliest indication of labor. Sepsis, however, even with suppuration in the wound, does not inevitably prevent further pregnancies or repeated Cesarean section.

Spencer had never met a case of rupture of the scar after Cesarean section. In his opinion it should not occur in an aseptic case properly sutured, but it may not be preventable in a septic case. Adhesions over the uterine scar in an aseptic case show a fault in operating and may be an important matter, possibly explaining some cases of sterility. In performing the operation he is accustomed to use carbolized floss silk of moderate thickness for the deep sutures and a continuous fine silk suture parallel to the incision by a fine, round, straight sewing needle, taking a double grip of the peritoneum and superficial muscle, so that the deep stitches are buried and no suture at all is shown. Catgut, he believes, should be absolutely condemned as a material for suture in Cesarean section.

Bride, in the Manchester Hospital, found that of 1920 cases treated by Cesarean section 96 had not subsequently become pregnant, and on analyzing the statistics the relative sterility is reduced to 34.7 per cent. Of the 96 cases, 55 per cent had some fever after delivery. There were 4 cases in which natural delivery was attempted after Cesarean operation, and of these 1 died. This patient had an ovarian cyst obstructing labor at her first parturition and was delivered by Cesarean section with the right ovariectomy. In the second pregnancy, as there was no pelvic contraction, labor was allowed to develop fully when the scar ruptured. The patient was immediately subjected to operation, but died from collapse and shock.

In closing the discussion, Holland stated that he could trace his cases after section in about 70 per cent. Kerr had 1 death in 18 cases, in which section was performed by the method which he described with transverse incision through the lower segment.

The reviewer's experience comprises three cases in which there has been a breaking-down or rupture of the scar after Cesarean section. One occurred in a negro woman admitted to the hospital after considerable labor, with a slight rise of temperature. She made a fairly good recovery after the operation, with a slight rise of temperature, and nursed her child. In the next pregnancy she came under the care of W. E. Studdiford, at Bellevue Hospital, in New York, and, as labor proceeded slowly, it was feared that the scar was overdistended or breaking down. On section, the scar was found greatly thinned and on the point of rupture. On careful examination at several points, apparently stitch holes, the tissues had parted.

Another case on whom section had been done was admitted to the hospital in labor without descent and engagement after being in the care of an outside physician for some time. There was a history that after considerable pain, the pains had suddenly ceased. Upon opening the abdomen, the lower portion of the scar had ruptured while the upper remained intact. The child's head had escaped through the rent and was dead. The mother recovered after hysterectomy.

In the third case the patient had section for neglected labor and had

been examined outside the hospital by a midwife. After delivery, the abdominal wound healed by first intention and there was a very slight, if any, elevation of temperature. The patient was taken away from the hospital by her husband against the advice of physicians and was made to sign a release, assuming all responsibility. She returned subsequently, again pregnant, not in good general condition; the abdominal walls were much relaxed, but with apparently the uterus in fairly good condition. The uterine muscle was flabby, but there was no evidence by palpation that the scar was not good. She was strongly urged to come into the maternity for labor. She visited the out-patient clinic several times and the warnings were always repeated. She was seen by the reviewer, who gave her definite instructions and stated the reason.

She was next brought to the hospital in a taxicab by a physician who had been summoned to her when in labor. He had found her in shock, with a statement that she had had some very strong pains which had ceased. Recognizing the gravity of the situation he had at once brought her to the hospital. On opening the abdomen, it was found that the uterus had ruptured completely through the uterine scar. A dead child was in the abdomen and the placenta had not separated. The patient was moribund and did not long survive. The uterus, tubes and ovaries were removed, and, on examining the specimen, it was seen that rupture had occurred through practically the entire extent of the incision.

These three cases were operated upon by the same method, namely, turning out the uterus from the abdominal cavity, covering the intestines with large compresses wrung out of hot sterile salt solution, opening of the uterus longitudinally through the upper expulsive segment, the delivery of the child and its appendages through the uterine wound, and if there was reason to suspect a possible infection the uterus was packed and drained by 1 per cent iodoform gauze. The three cases did well so far as primary union of the abdominal wall was concerned. They were operated upon by different operators, but by the same method.

It is evident that at present the question of danger of rupture of the scar in subsequent pregnancy after Cesarean section is of great importance in obstetrics. The majority of opinion holds that, for the uterine muscle, silk is the best suture; some urge a continuous suture, because they believe that in this way the muscle can be most smoothly brought together, a more perfect union secured and thus a stronger scar. Furthermore, this continuous suture prevents the formation of dead spaces in which blood or serum may collect. Catgut is used to close the peritoneal covering of the uterus. All operators agree that the avoidance of infection is of primary importance; hence, cases which have been under care by those who do not practice strict asepsis must always be considered as suspicious. While it is not justifiable to sacrifice the uterus in all of these cases it is certainly the duty of the obstetrician who operates upon them to take additional precautions to drain the uterus and to prevent hemorrhage.

A question of the site of the incision of the uterus cannot be said to be fully determined. It must be admitted that the extraperitoneal operation is practically so rarely possible that it may be disregarded.

Cervical operation can be done through the lower segment and cervix by opening the peritoneum, but the operator may choose to perform his operation through a peritoneal fistula, stitching the uterus and parietal peritoneum together before opening the womb. The operation through the cervix and lower segment has not yet been practised sufficiently extensively to enable us to judge accurately concerning its merits, especially as regards the subsequent rupture of its scar. What has already been said in abstracting draws attention to the danger of wounding the connective tissue in the vicinity of the bladder and thus bringing about an infection of this tissue or of the abdominal wall.

A further question arises: What is the duty of the obstetrician in cases in which it is wisest to deliver by section and there is every reason to believe that the patient is infected? Recognizing the fact that the body of the uterus is the point of greatest danger, shall the uterus be sacrificed to save the life of the mother? Here the circumstances of the case are of great importance. If the woman is a young primipara the power of procreation should not be removed; the uterus should be drained and sutured, with the hope that serious infection will not develop. If the patient is a multipara and near the end of her reproductive life then hysterectomy, leaving the stump outside the abdominal cavity in the lower end of the abdominal incision, should be chosen. Of the good results in securing permanent health for these patients no one can doubt who has ever examined such a patient a year or more after recovery. The cervical stump is firmly fixed and the vaginal and pelvic tissues are drawn up so high and so firmly that prolapse is impossible. The patient's general condition, so far as the pelvis is concerned, is exceedingly good.

A comparatively brief, but interesting, review of 300 classic Cesarean sections is given by Richter.⁴⁷

THE PUERPERAL STATE.

Condition of the Nervous System in Parturient Women. Poenstan⁴⁸ discusses this subject in a thorough manner. His study has been made in the Clinic for Psychiatry and Nervous Diseases in Kiel. In studying one of these cases one must consider as to whether the patient was mentally overcome by the occurrence of labor and endeavored in any manner to conceal the occurrence of labor. If she has been delivered, the place where delivery occurred must be considered, the method and course of delivery, what assistance, if any, the patient had, how competent was her care and the psychic condition of the woman aside from gestation.

It must, in general, be recognized that the nervous condition of the parturient woman cannot be considered normal. A very slight shock is sufficient to overthrow the psychic balance and produce a pathological condition; such a shock may come from an abnormal labor or from some psychopathic condition existing prior to labor. Where disturbances of the nervous system complicates labor they usually appear in the form of

⁴⁷ *Archives f. Gynäkologie*, 1920, No. 112, p. 70.

⁴⁸ *Monatsschrift f. Geburtshilfe*, 1920, iii, No. 51, 198; iv, No. 51, 256.

unconsciousness, great excitement or convulsions, delirium, obtunding to the mind and paralytic or hysterical manifestations. Eclampsia is accompanied by severe disturbances of the psychic condition. Puerperal fever very often results in delirium. The strain of parturition itself is sufficient frequently to arouse to activity latent psychopathic states.

When the question of child murder arises, one must remember that the parturient woman is in an unstable condition, and that if she be overcome by shame of illegitimate pregnancy this may be sufficient to furnish the impulse for the crime. It is often very difficult to critically analyze such a case and to distinguish between overwhelming impulses and deliberately formed purposes.

In alluding to the tremendous psychic disturbances which the pains of labor may cause, the writer alludes to cases in which during severe labor pains patients have struck their head against the wall of the room, torn out the hair in agony, endeavored to pull the child out from the vagina and given evidence of temporary delirium caused by pain. He states a case in which, in the agony of labor, the woman threw herself out of a window and another where the patient in labor sprang through a glass window, cutting herself severely and falling some distance to the ground. Women in labor have not only thrown themselves from windows, but in a few instances have endeavored to drown themselves. In one case a woman who had been in long and tedious labor for three days endeavored to hang herself with an apron.

Possible the tremendous psychic disturbance of labor finds its fullest outlet in those who practice Cesarean section upon themselves. A number of these cases are on record, many of which were not followed by death of the mother, and sometimes accompanied with saving of the life of the child. Self-inflicted Cesarean section is a reversion to primitive instinct. Of similar nature are those cases in which the mother endeavored to destroy the child as soon as it was born. In these conditions of intense excitement amnesia develops which is usually of short duration. The excitement produced by labor is termed by many neurologists transitory mania, and may last from five minutes to half an hour, and become especially violent at the moment of delivery. In pregnant women suffering from chorea the institution of labor may be accompanied by great psychic disturbances. So epileptic and hysterical women may be thrown into convulsions by labor. In one instance a woman became hysterical and in a semiconscious state fourteen hours before delivery, and so continued four days after the birth of the child, with complete amnesia. In another the patient was hysterically unconscious during labor, which was terminated by forceps, and only aroused in fright when the physician prepared to leave the hospital. In another patient the condition of hysterical unconsciousness began during the period of dilatation with great motor excitability. The patient became speechless, and although unconscious seemed greatly aroused. One-quarter hour after the birth of the child the patient spoke in a disordered manner; a half-hour after the birth of the child she recognized where she was, but had complete amnesia regarding labor and its details. In this case

there was no hemorrhage, infection or special complication, nor did the patient give a history of previous hysteria or epilepsy.

The psychoses of eclampsia are especially important for mother and child; while apparently unconscious the patient may develop labor, and not attracting attention, the death of the child may follow lack of medical help. A patient who had previously been mentally disturbed was taken with eclamptic convulsions during labor, locked herself in a room and, when found by the police, was lying unconscious, the child dead because of rupture of the umbilical cord. The presence of edema, albumin and casts in the urine and the bitten condition of the tongue made the diagnosis of eclampsia plain. A patient having albumin in the urine became comatose, with greatly dilated pupils, just before the occurrence of labor. She had endeavored to strangle herself; in order to deliver her with forceps, it was necessary to use anesthesia, and as soon as this ceased she became violently excited, which lasted for about ten hours. She finally became calm and remembered her attempt at suicide with horror.

Eclamptic patients always have amnesia, which may begin five weeks before labor. This amnesia has been divided into four varieties: (1) In which the patient does not remember persons, dates or circumstances before labor; (2) in which she has no knowledge of labor itself; (3) in which for a long period before the outbreak of eclampsia her memory is a blank on every subject; (4) when amnesia develops but a short time before eclampsia convulsions.

The destruction of the child may occur at any period of mental disturbance complicating labor, often with melancholia, in mania and in the excitement which imbecile patients have during labor, while other patients mentally disturbed before pregnancy show a remarkable development of maternal affection during and after childbirth. Patients mentally deranged frequently have quick and easy labors, especially those suffering from paralytic dementia.

In caring for these patients one must carefully protect them from every unfavorable and disturbing influence which may affect the mind; loud noises, confusion and excitement must be absolutely prevented. Attention must be given to the general physical condition, and, if necessary, stimuli should be given during labor. If a patient is epileptic an effort should be made to thoroughly treat her with bromides or luminol during pregnancy to lessen the violence of epileptic convulsions during labor. The appropriate treatment of eclampsia and disturbance of the kidneys in these cases is clearly indicated. The use of morphine, avoidance of hemorrhage and stimulants given for condition of unconsciousness are all indicated. Alcohol should be used very sparingly as a stimulant, especially in epilepsy or neuropathic cases. To quiet excitement, duboisine, scopolamine and hyseamine are indicated. When the patient is uncontrollable during labor brief anesthesia may be necessary. The use of forceps is often indicated to save the child and terminate the mother's excitement. In eclampsia, if thought best to terminate pregnancy it should be done as rapidly and painlessly as possible. Where

delirium in pregnancy and parturition is caused by fever, the infection underlying the fever should receive attention. Small doses of pyramidon often control temperature and quiet the patient. Where the condition is purely psychic and drugs are found of little avail the general management of these patients is indicated.

Interesting medico-legal question may arise concerning labor and its consequences in these cases. If the patient is unconscious or mentally disturbed she cannot give permission for operation, and hence the physician must be sure of his ground in undertaking radical interference. It is often difficult to know whether a neurotic patient is mentally responsible during labor and whether she is thus responsible for consent for treatment or for the death of the child. The death of the child by overlying by the mother may not be a deliberate murder. It may be difficult to prove that the woman intended to injure the child. Various civilized countries differ in holding the unmarried mother to strict accountability for injury to her offspring.

The phrase "during birth" is applied to the time when the child ceases to obtain oxygen through the placenta and the separation of the umbilical cord. When the phrase is used "immediately after labor" it is necessary to know accurately, if possible, at what time the abnormal mental condition of the mother developed. If the mother was unconscious before labor or at the beginning of labor, she may not be responsible for what has happened to the child. In estimating the circumstances of fetal death, one must take into account the married or unmarried condition of the mother and degree of shame, shock and remorse, which is often the case. The question arises as to the responsibility of the mother unmarried who deliberately makes no preparation for confinement, conceals the fact of her pregnancy, summons no assistance when taken in labor, remains alone and makes no effort to preserve the life of the child. On the other hand cases are sometimes observed in which the mother, apparently normal, will destroy the child in a moment when no one is observing her. In 58 cases in which the death of the infant was intentional in the mother there was evidence of deliberate and previous intention in only 1, while a neurologist of large experience had observed but 6 cases in which the child had deliberately been destroyed. In many of these cases the destruction of the child is followed or accompanied by effort at suicide on the part of the mother, and this may occur as late as three days after the birth of the infant. In many of these cases failure to conceal illegitimate pregnancy and the birth of an illegitimate child seems to be the motive for the destruction of the infant.

While the writer does not mention the subject of the late war as given examples of deliberate destruction of infants, women taken by enemy soldiers and impregnated have given birth to children, and in some instances have deliberately destroyed them; in none of these cases in the knowledge of the reviewer has a woman been convicted of child murder.

Poensgan's paper is a carefully prepared and minute review of the subject, and will well repay study by obstetricians. His statistical material is considerable and he is able to give the results in one instance

of the study of unconsciousness developing during 2200 cases of labor; so extensive material adds weight to his conclusions.

In the opinion of the reviewer, this paper is especially timely in view of the general effort of obstetricians to endeavor to conduct labor in as painless a manner as possible. In order to correctly recognize and estimate the action of analgesic and anesthetic drugs during labor the obstetrician must understand the psychology of labor and the normal reaction to labor of the psychic elements in the patient. An effort to produce amnesia is an imitation of hysteria developing during labor. The stimulating effects of anesthesia in promoting vigorous uterine contractions and shortening labor illustrate the value of relieving the automatic mechanism of parturition from the depression occasioned by psychic disturbances. The mental disturbances produced by the toxemia of pregnancy is familiar to obstetricians, and the mania following and accompanying eclampsia is not infrequent. The practical conclusions to be drawn from this paper and obstetrical experience are that parturient women are in a condition of psychic instability. That she should be guarded during labor from excessive suffering, from depressing influences and from bad results of long-continued and painful parturition. In an emergency appeal may be made, in healthy women, to normal maternal impulses to secure coöperation in matters of treatment. Obviously, psychoanalysis should be included in the study of parturition and may be of decided value.

Is Every Puerperal Uterus Infected? When one considers the fact that the uterus is in direct connection with a canal opening upon the surface of the body, and so situated and surrounded that bacteria can readily enter, it seems doubtful whether the uterus is ever during parturition and the puerperal state in a condition of absolute sterility. Loeser⁴⁹ has studied this question minutely by bacteriological methods. He quotes extensively the results of others which in former times have likewise endeavored to solve this problem by bacteriological examinations. His results are carefully tabulated, and the uterus was examined at various periods of the puerperal period; his study seems to justify the conclusion that in every normal puerperal period bacteria make their way from the vagina into the uterus. The placental site is evidently the best culture-ground for these germs. On the first day after labor bacteria are found at the internal os, on the second day at the placental site, so that the puerperal uterus may be considered as infected at this time. This may happen as late as the fifth day and a slow or rapid invasion of bacteria does not depend so much upon the character of the bacteria as upon the condition of the tissues of the birth canal. Anaërobic bacteria make their way more rapidly than others. All the micro-organisms found in the puerperal uterus of patients having fever are also found in the normal uterus. The activity of these germs seems to depend not so much upon their presence as upon the condition of surrounding tissues, and no difference can be observed in the behavior of microörganisms thought to be pathogenic. A long-continued labor pre-

⁴⁹ *Zeitschrift f. Geburtshülfe*, 1920, No. 82, iii, 577.

disposes to the rapid increase of bacteria in the vagina and in the uterus, and distinctly lessens the resisting power of the maternal tissues. The length of time elapsing from the rupture of the membranes to the birth of the child and the length of time occupied in delivery of the placenta do not seem to be of vital importance. The duration of labor is important because it lessens the resistance of the patient. Gonorrheic and anaërobic bacteria grow better in the uterus than in the vagina, but in normal puerperal patients the bacteria of the vagina grow equally well in the vagina, cervix and in the uterus.

The reviewer has long believed that the facts stated in this paper are abundantly borne out by clinical observations. It would otherwise be impossible to explain the remarkable recoveries from neglected and complicated labor in the cases of robust and hard-working women and the rapidly developing morbidity and mortality in women whose power of resistance is lessened by hemorrhage, physical degeneracy and frequent and fruitless interference with labor.

Extra-genital Septic Infection in Puerperal Patients Producing Death in the Puerperal Period. Schmitt⁵⁰ calls attention to the fact that there are sources of infection in the parturient women which may produce death after the birth of the child independently of puerperal septic infection. In 20,000 births there occurred 5 deaths from infectious puerperal processes after normal labor. One woman had gonorrhea and 2 had hematogenic infection proceeding from the tonsils, and 2 had either an infection with exogenic germs introduced by examining finger or had an autogenous infection. The writer calls attention to the possibility of infection in the puerperal period through the blood stream; this may happen from pneumonia, arthritis, typhoid ulceration of the intestines and *Streptococcus angina*. There are a considerable number of cases of the last which have been accurately studied and recorded.

The writer reports 3 deaths from septic infection in the puerperal period independently of childbirth. In 1, chills and fever developed on the fourth day; on the sixth day the patient's tonsils were red and swollen the genital tract and abdomen remaining normal. On the eighth day the abdomen was distended, on the ninth day the distention increased, the uterus was not tender and on the tenth day death occurred. A thorough autopsy showed without doubt that streptococcus from the tonsils had entered the blood stream, and among other lesions had produced a septic peritonitis; the uterus and surrounding tissues were not septic.

The second patient died on the twelfth day after birth from general septic infection, with fever and pain in the left thigh and swelling and tenderness in the lower third. Autopsy failed to show clearly the original point of infection; the cavity of the uterus was perfectly clean and no evidence of infection in the genital tract. There was no thrombosis in the veins of the thigh or in the veins of the pelvis; there were vesicles on the epidermis filled with bloody fluid.

The third case developed a distended abdomen and peritonitis on the

⁵⁰ Monatschrift f. Geburtshülfe, 1920, ii, No. 52, 117.

seventh day after normal labor. Abdominal section showed the coils of intestines distended, the peritonitis and exudate present containing streptococci. Death followed on the fourteenth day. At autopsy, the uterus and placental site were clean and showed no sign of infection; the parametria showed vessels filled with pus. There was thrombosis of the right femoral vein, hemorrhagic bronchitis, right lung adherent to the pericardium, mucous membrane of the trachea reddened and swollen, lymphatic glands about the bronchi and trachea were swollen and contained points of bright red hemorrhage.

Another case is reported in which the patient came to the Maternity Hospital desiring attention because one of the children was ill with scarlatina. She was admitted, was isolated and a child was born three hours later. No examination or disturbance of the birth canal had been made. On the fourth day symptoms of infection developed, on the eighth day peritonitis, with death on the tenth day. An autopsy could not be obtained; circumstances point unmistakably to infection referred to the streptococcus of scarlatina.

DISEASES OF THE THORAX AND ITS VISCERA, INCLUDING THE HEART, LUNGS AND BLOODVESSELS.

BY O. H. PERRY PEPPER, M.D.

DISEASES OF THE HEART AND BLOODVESSELS.

Capillary Contractility as an Important Factor in the Circulation. It has only been within the past two or three years that evidence has been advanced which satisfactorily demonstrates that the older view, which limited vascular control to the arteries and arterioles, was not the whole of the story. Within this short period our views have been considerably altered by observations of undoubted accuracy and importance. In brief, this newer conception of capillary activity endows the capillary and the venule with independent tonus and ability to undergo constriction and dilatation. In a sense this hypothesis is far from recent but its demonstration is new, and so is the appreciation of its importance and wide applicability.

It is to Krogh,¹ of Copenhagen, that the stimulus to the development of this new hypothesis is due. He perfected a method of studying the living capillaries in muscle, and as a result of his observations came to the conclusion that the capillaries are not merely passively dilated by blood-pressure but constantly perform active changes in caliber. Furthermore, not all the capillaries in a given area of muscle are open and filled with circulating blood at one time, nor are the open capillaries equally dilated. Apparently, as a result of some unrecognized stimulus, probably chemical, capillaries open and close and the blood is accordingly shunted from one set of channels to another, perhaps in accordance with the needs of the various areas. Such changes appear to occur in capillaries supplied by one and the same arteriole. This variation in capillary flow may be readily observed by the so-called Lombard method of placing a drop of oil on the skin overlying the matrix of the finger-nail and examining with a fairly low power of the microscope. Krogh² also used the tongue of the frog for studying the intermittency of the flow in individual capillaries, and the effects of various chemicals when applied directly.

Krogh concludes that capillary tonus is independent of blood-pressure and is not of nervous origin but must depend upon some constituent of the blood. Furthermore, he feels that the evidence excludes the possibility that oxygen is the substance determining the tone of the capillaries.

Hooker³ has also done important work on this subject and has summed up the present status of our knowledge in an excellent review.⁴ He points out that such changes in capillary lumen, while ordinarily balance-

¹ *Journal of Physiology*, 1919, lii, 409 and 457.

² *Ibid.*, 1920, liii, 399.

³ *American Journal of Physiology*, 1920, liv, 30.

⁴ *Physiological Review*, 1921, i, 112.

ing one another in different parts of the body, might, under special conditions, exert a profound effect both upon the distribution of the whole blood and upon its partition between corpuscular elements and plasma. The part played in "shock" by dilatation of large capillary beds may be of great importance, and, on the other hand, marked increases in the red cell count (polycythemia) may be due, as it has been suggested by several writers, to alterations in capillary lumen and concentration of the blood. Broadly speaking the capillary bed responds by dilatation to chemical stimuli, and, by constriction, to nervous stimuli. Hooker suggests that nervous control may act over the capillary beds of the body as a whole while chemical factors are usually local in character, although, of course, the chemical factor may be in the circulating blood.

Undoubtedly these preliminary investigations will be followed by many more along a variety of lines, and many important additions to our present facts will be made. The extremely interesting and important observations of Richards on glomerular function in the kidney are closely related to Krogh's work and fully confirm the soundness of the general principles which he established. Perhaps from the circulatory aspect the most important point which this new hypothesis introduces is the necessity of our revising our conception of peripheral resistance to include the capillary, a factor which may prove to be of unsuspected importance.

Studies of the capillaries in the affected part in a case of Raynaud's disease were carried out by Halpert.⁵ This author states that the studies were made by means of Weiss's method. This is the same method which is mentioned above, of observing the capillaries of the matrix of the nail after rendering the skin transparent with a drop of oil. Weiss's earliest papers on the subject were in 1916⁶ and 1917⁷, and in the latter of these he quotes the earlier work of Lombard.⁸ It is by Lombard's name that the method is usually designated in the literature of this country. Apparently, Weiss in no way improved or modified Lombard's method and there is little excuse for the use of his name in connection with it. Halpert observed the capillaries both between attacks and during an attack. The observations were not apparently very definite nor conclusive.

Endocarditis. The classification of the various varieties of endocarditis is in a somewhat confused state and the terminology is in many respects misleading. Equally bad is the state of our knowledge concerning the interrelationships between rheumatism, chorea and endocarditis. Some authorities use the terms benign and malignant when referring to acute endocarditis and place "recurrent infective endocarditis" in a separate group. Others object to the term chronic endocarditis as it is usually employed, pointing out that in such cases there is present only the valve deformity which has resulted from the extinct endocardial infection.

⁵ Zeits. f. d. ges. exp. Med., 1920, xi, 9.

⁶ Deutsch. Arch. f. klin. Med., 1916, cxix, 1.

⁷ Münch. med. Wchnschr., 1917, lxiv, 609.

⁸ American Journal of Physiology, 1911-12, xxix, 335.

Ivy Mackenzie,⁹ in a recent system article, states that the subject will be considered under the following divisions: (1) Simple verrucose endocarditis; (2) acute ulcerative endocarditis; (3) subacute ulcerative endocarditis; (4) chronic endocarditis. Later a heading "Acute Infectious Endocarditis" is introduced. Still other writers avoid the difficulty by designating the causative organisms, as, for example, Streptococcus endocarditis or Pneumococcus endocarditis. The term rheumatic endocarditis is frequently met with, and while having some justification leaves much to be desired. The term "recurrent," referred to above, is ambiguous, for we see two different types of endocarditis in which recurrence of infection occurs. The first of these is seen in the secondary attacks of endocardial trouble of rheumatic origin which may follow, even years later, after the primary attack. The other recurrent form is that to which this term is usually applied. This group is characterized by the later implanting on a valve previously injured by simple, benign or rheumatic endocarditis of a secondary infectious process due usually to the Streptococcus viridans and ultimately always fatal. These are the cases sometimes referred to as "slow malignant" or "subacute" endocarditis. That the streptococcus in these cases is not to be confused with the form which by some is claimed to be the etiological agent in acute rheumatic fever seems certain at this time.

Kinsella¹⁰ presents the subject from still another aspect. He divides all endocarditis into two main groups, the bacterial and the non-bacterial. Of the former we have several varieties, the clinical course of each of which depends on the invading organism. When staphylococci or gonococci invade the course is short and "malignant," and death occurs usually within a month. When a streptococcus is implanted the course is "subacute," but death is certain. Kinsella classifies the endocarditis produced by rheumatism as of a non-bacterial type. Attended as it is by fever we are prone, he says, to regard it as bacterial in origin. In rheumatic endocarditis the lesions are hard, small, verrucose nodules which are homogeneous and hyaline-like in composition and have no bacteria. On the other hand the vegetations of bacterial endocarditis are soft and friable and composed almost entirely of bacteria. All bacterial types may ulcerate. The blood cultures in bacterial endocarditis show a remarkable constancy; if a culture shows 50 to 300 colonies per cubic centimeter one day it will usually show the same count for weeks. Just before death the bacteremia becomes intense. It is on the blood culture that Kinsella places the greatest importance. "Before a diagnosis of bacterial endocarditis can be made the bacteremia must be found to be constant." The finding in one blood culture of a few colonies of green streptococci and then none in subsequent cultures is not sufficient evidence to prove an endocarditis bacterial. Such a finding in a rheumatic case would not persuade Kinsella to consider the endocarditis other than non-bacterial. The cause of rheumatism is unknown, while it is well known that the green streptococcus is a common variety in human mouths.

Kinsella further states that no case of true bacterial endocarditis

⁹ Oxford Medicine, 1920, ii, 296, Oxford University Press.

¹⁰ Medical Clinics of North America, November, 1920, iv, 813.

has recovered. To speak of such types of heart infection becoming bacteria-free is to assume much. In such instances in which this appears to have happened Kinsella would doubt the correctness of the primary diagnosis. Once, however, the heart valve has been seriously injured by a previous disease an invasion of the blood stream by streptococci from the mouth, incited perhaps by tonsillitis, may result in implantation on the diseased valves.

These apparently somewhat arbitrary views are of interest and give us food for thought even though we may be unwilling to accept them in detail.

An interesting side-light is thrown on the ETIOLOGY OF ACUTE ARTICULAR RHEUMATISM by a report by Grenet.¹¹ He observed five distinct epidemics among groups of soldiers. The outbreaks occurred within a zone of trenches occupied by certain regiments and later appeared in their respective rest camps where these units were sent. In these rest camps other troops became infected in their turn, apparently from contact, since later occupants of the same quarters failed to become infected. Grenet details the following case history as evidence of the contagious character of acute articular rheumatism. A soldier who had not had rheumatism, but who was a member of a regiment in which an outbreak had occurred, was detached to another command and shortly after was wounded and admitted to a hospital. Twenty-six days after admission to the hospital he developed clear-cut acute rheumatism, and six days later two wounded soldiers occupying adjacent beds had similar attacks.

This report would suggest a much greater specificity and contagiousness of acute articular rheumatism than is usually considered likely. If such is true it seems probably that tonsillar infection is of importance as the portal of entry or the focus of infection.

TONSILLITIS AND ENDOCARDITIS. Although we may have to admit that the cause of acute articular rheumatism and of "rheumatic" complications, such as chorea and endocarditis, is unknown, yet the relationship of disease of the tonsils to acute rheumatism is very suggestive. In three ways may the diseased tonsil apparently be related to endocarditis: (1) as the starting-point of the initial attack, whether this takes the form of rheumatic fever, chorea or endocarditis; (2) the tonsillar disease may apparently be related to recurrent attacks of similar or identical trouble; and (3) the tonsil seems to act as a portal of entry for the streptococcus which later may implant itself on previously diseased valves. The reviewer does not see any good reason for allowing our uncertainty concerning the actual cause of acute rheumatism to lessen our appreciation of the importance of disease of the tonsil as a factor, and, in children perhaps an essential one, in the etiological chain.

Last year an abstract of Lambert's article appeared in this review.¹² Lambert suggested, from a study of the incidence of acute rheumatic fever at Bellevue Hospital, that the decrease in the frequency of this condition might well be due to the influence of improved dental care

¹¹ *Gaz. des hôp.*, 1920, xciii, 5.

¹² *PROGRESSIVE MEDICINE*, September, 1920, p. 33.

and the removal of diseased tonsils. Evidence along the same line has been advanced by St. Lawrence¹³ from a follow-up study of 94 children, each of whom had suffered from acute rheumatic fever, chorea or allied rheumatic manifestations, and each of whom had subsequently undergone a complete removal of the tonsils. During an average period of three and a half years after the operation was performed these patients were followed. Of the 42 cases who had had one or more attacks of rheumatic fever before the tonsils were removed, 35 showed no recurrence afterward. Forty cases had had chorea before the tonsillectomy and there was no recurrence after the operation in 20 cases, or 50 per cent. There were 58 cases of organic disease of the heart in the series. Twelve of these patients had suffered at least one attack of cardiac failure before the tonsils were removed. One patient suffered one attack afterward. Further, the exercise tolerance in the cases of cardiac disease and the nutrition and general health seemed to be favorably influenced by tonsillectomy in the instances in which indications existed for the removal of the tonsils. In other words, as Lambert said in the discussion of this paper, St. Lawrence's point is that if you get the tonsils out rheumatism does not recur.

In Ledford's¹⁴ analysis of 250 cases of acute endocarditis in children he found that tonsillitis was present in the majority of the cases in which there was chorea or rheumatic fever associated with the endocarditis. In 30 cases, or 12 per cent, however, tonsillitis was the only associated condition. Adding these groups together it is found that tonsillitis was present in the majority of the 151 cases (60.4 per cent) with rheumatic fever; in the majority of the 36 cases (14.4 per cent) with chorea and in the 30 cases (12 per cent) of tonsillitis. In other words, of the 250 cases of acute endocarditis the majority of 217 cases (86.8 per cent) had an associated tonsillar trouble.

Parkinson, Gosse and Gunson,¹⁵ in an interesting article which will be referred to again under Diseases of the Myocardium, mention that of 50 cases of acute rheumatism there was a history of sore-throat accompanying the attack in 16 cases and enlarged tonsils were present in 30 of the 50 patients. In 26 cases the cervical glands were easily palpable.

Further evidence comes from the bacteriological side. Richards¹⁶ in 16 cases of chorea found some evidence of infection with *Streptococcus viridans* in all but 3 cases. In 9 cases the tonsils were found to be foci of *Streptococcus viridans* infection, in 8 foci were found about the teeth and in 5 cases in the nose. The complement-fixation with *Streptococcus viridans* antigen was positive in 13 cases and negative in 3. The blood cultures showed *Streptococcus viridans* positive in 5 and negative in 11 cases.

The evidence which has been grouped together here in this brief manner may not seem to do justice to a topic as important as this one, but it is scarcely within the scope of a review such as the present to do

¹³ Journal of the American Medical Association, 1920, lxxv, 1035.

¹⁴ American Journal of Diseases of Children, 1921, xxi, 139.

¹⁵ Quarterly Journal of Medicine, 1920, xiii, 363.

¹⁶ Journal of Bacteriology, 1920, v, 511.

more than touch on the important and suggestive aspects of a subject. The articles chosen for mention should reflect the current writing and views, even if they seem to be at variance with older and more established beliefs.

SUBACUTE BACTERIAL ENDOCARDITIS. *Discussion of its clinical significance and course.* At the eighty-eighth annual meeting of the British Medical Association the Section of Medicine met to discuss this subject. The various articles forming this symposium deserve to be read in full.¹⁷ The chairman (Dr. Thomas Lewis), in opening the meeting, emphasized the importance of the subject, and stated that one reason for giving it prominence was that the disease often escaped recognition. We were too apt to look for high fever when in subacute bacterial endocarditis the temperature was not conspicuously high; often there was no fever for considerable periods. A more important reason for the disease being overlooked was the misinterpretation of two signs, namely, pallor in aortic disease and clubbed fingers. Pallor in aortic disease should not be explained away as due to the aortic regurgitation; this is incorrect, it usually being due to associated infection. Clubbing of the fingers while sometimes, as in congenital heart disease, a simple associate of valvular disease or congestion, is in adults who present heart disease much more frequently associated with infection. These signs are, of course, not diagnostic, but are very suggestive of cardiac infection.

Sir Thomas Horder was the first speaker. He commenced by defining subacute bacterial endocarditis; under this heading is not to be included that form of endocarditis which accompanies acute and subacute rheumatism, nor that form of endocarditis which is but one part of an acute pyemia and in which the heart lesion is secondary to rather than responsible for the systemic infection or septicemia. The disease to which the term subacute bacterial endocarditis may be properly applied has more or less of the following features:

"The onset is most often insidious; the general symptoms include loss of strength and tone, a sallow complexion with anemia, moderate loss of weight, and fever; the heart gives evidence of endocarditis at some time or other in almost all cases, and in the majority there has been previous valve injury; widespread arterial embolism takes place; in most cases blood cultures are positive, the isolated bacterium being either a short streptococcus, much less often Pfeiffer's bacillus, and rarely a microorganism difficult of identification, but in all cases the microbe is of low pathogenicity. The course of the disease is slow but progressive, and though remissions occur it is, once established, almost invariably fatal. The total duration of the illness is from three months to two years, with an average duration of six months; death occurs from toxemia, from heart failure, from uremia or from cerebral or coronary embolus. The postmortem findings include a vegetative endocarditis on the valves or wall of the heart, with little or no ulceration, and widespread embolic infarction without suppuration. As a result of the embolic process there is found a form of glomerular nephritis more or less characteristic of the disease."

¹⁷ British Medical Journal, 1920, ii, 301.

Horder places the frequency of this disease as 1 in 200 of the patients admitted to the medical wards of a large general hospital. Most of the cases occur between the ages of fifteen and fifty and half of them between twenty and forty. In about half the cases met with there is a history of acute or subacute rheumatism or of chorea, but between the occurrence of the rheumatism and the onset of the endocardial infection there has usually been an interval of several years, very often years of good general health. The heart valve damaged by previous rheumatic inflammation is not merely cicatrized but presents also an increased vascularity which may be the determining factor in the establishment of the secondary infection.

The onset may be most insidious; unexplained fever, atypical rheumatic pains or even less definite symptoms may exist for some weeks without other evidence to suggest the true condition. In other cases a frankly embolic event first draws attention to the serious nature of the trouble: sudden pain in the left flank followed by the discovery of an enlarged and tender spleen; pain in the arm with temporary obliteration of the radial pulse on that side; blood in the urine, complaint of defective vision due to retinal embolism—to name some of the more common instances. Occasionally a positive blood culture from a patient suffering with an unknown malady first suggests to the doctor the nature of the illness under investigation. Once established four cardinal signs of the disease occur; these in the order of their importance from the point of view of diagnosis are: Multiple arterial embolism, endocarditis, the isolation of a bacterium from the blood stream and fever.

Horder states that since we have become more familiar with the disease the confirmatory evidence of a positive blood culture is less essential to a correct diagnosis. He believes that a varying degree of systemic blood infection exists throughout the whole course of the disease and that a series of negative blood cultures does not indicate that the vegetations are "bacteria-free."

Libman was in agreement with Horder's viewpoints and occupied himself chiefly with pointing out some of the differences between "rheumatic" endocarditis and subacute bacterial endocarditis. Some of these have been compared in the following table:

	"Rheumatic" endocarditis.	Subacute bacterial endocarditis.
Valve lesion . . .	Small, firm, covered by endothelium	Vegetative.
Heart muscle . . .	Aschoff bodies	Bracht-Wachter bodies.
Pericarditis . . .	Frequent	Rare.
Kidneys . . .	Nothing characteristic	Characteristic glomerular lesions.
Skin . . .	Often red over joints; erythema nodosum common; petechiæ not seen	Never red over joints; erythema nodosum does not occur; petechiæ common.
Nodes . . .	Subcutaneous, not tender	Cutaneous, tender (Osler's nodes).
Embolism . . .	None.	Common.
Bacteria . . .	Occasional <i>Streptococcus viridans</i> ; no positive complement-fixation	Uniformly positive findings; <i>Streptococcus anhemolyticus</i> , 95 per cent; <i>Bacillus influenza</i> , 5 per cent.
Point of attack . .	Previously normal valves	Previously damaged valves.
Recovery . . .	Frequent	Four complete recoveries in 300 cases.

Libman in describing certain cases he has seen which have actually become bacteria-free says: "Clinically these patients, besides presenting some of the symptoms seen in the active (bacterial) stage, such as petechiæ (the white centered ones being the most valuable for diagnosis), a tender sternum, moderate splenic enlargement, café-au-lait color of the face, etc., have certain clinical features that are distinctive. Some develop renal insufficiency and die of uremia, some die of progressive anemia and others of embolism. In some a very marked enlargement of the spleen is found, and these patients are usually suspected of being victims of Banti's disease. A few present a dark-brown color of the face that is distinctive. It is to be noted that some or nearly all these features may be found grouped in a single case." These bacteria-free cases are not rare in Libman's experience, but the prognosis is little better, for although they may spontaneously become bacteria-free yet they die of after-results.

Poynton advanced the view that rheumatic endocarditis is not bacteria-free in its early stage and that subacute bacterial endocarditis is not a special disease, but a phase of cardiac infection resulting from various causes, one of the most important being the rheumatic. His explanation would be that the heart never really recovered from the early rheumatic attacks but that unhealthy bacteria-containing foci were left in the valves, which, when the health and resistance were lowered from some cause, became locally virulent, flared up and caused the final catastrophe of subacute bacterial endocarditis.

Coombs associated himself with Poynton in the discussion and emphasized the fact that he had seen fatigue and privation quite definitely predispose to the development of subacute bacterial endocarditis. Gow continued the discussion and drew attention to the fairly frequent occurrence of leukopenia in this group of cases. Sterling emphasized the ability of these patients to continue their usual activities until but a short period before their death. In his series of 38 cases 95 per cent showed pallor, 76 per cent clubbing of the fingers, 81 per cent enlargement of the spleen, 58 per cent petechiæ, 39 per cent gross embolic phenomena. Gibson drew attention to the other possible causes of petechiæ and stated that the point especially to be relied on, however, in the diagnosis of endocarditis is successive crops appearing from day to day, the earlier ones fading as compared with the later. He believes that if a positive blood culture be obtained in these cases the outlook is hopeless. In the general discussion which ensued a number of other members took part; the symposium closed with a reply to the discussion by Sir Thomas Horder. Altogether this was a most interesting and instructive meeting. Fifty-five cases of subacute "infective" endocarditis were very carefully studied by Cotton¹⁸ and [recently] reported. He also has been impressed by the fact that this condition is not a rare one. It was seen in 8 per cent of patients with gross valvular disease attending a special heart clinic. In the diagnosis, Cotton lays stress on the same set of symptoms and signs that have been discussed above; he

¹⁸ British Medical Journal, 1920, ii, 851.

lays chief reliance on gross valvular disease, pallor, enlarged spleen and clubbing of the finger-tips. In his series the spleen was easily palpable in 48 of the 55 cases. One of his conclusions is worthy of special mention: "Aortic regurgitation is the type of valvular disease usually seen in this disease; it is rare to find the mitral valve alone involved." This is interesting because of the belief that "rheumatic" endocarditis frequently affects the mitral valve alone, and, as we have seen, it is upon the valve damaged by a previous rheumatism that subacute infectious (infective) endocarditis is believed to be implanted. Cotton concludes that the average duration of the disease is less than fourteen months, but that death may occur within two months from the onset of symptoms. The disease is always fatal.

CASES OF SUBACUTE INFECTIOUS ENDOCARDITIS. "*Meningitic Form of Malignant Endocarditis of Slow Course.*" Under this title Lereboullet and Mouzon¹⁹ describe a typical case of subacute infectious endocarditis in which the picture was confused by cerebral symptoms. At first a transitory left-sided hemiplegia developed and headache of great intensity led to the suspicion that a meningitis was present. Later, however, the true diagnosis became evident and at autopsy the characteristic lesions were found on the heart valves and streptococci were demonstrated. The only cerebral finding at the postmortem was a small area of recent hemorrhage over the left frontal lobe.

Achard and Rouillard²⁰ use much the same term, "Malignant Endocarditis of Slow Form," in a description of the two cases of subacute infectious endocarditis. One of the cases is typical, the other unusual in that apparently the infection attacked a healthy valve. This was evidenced not only by the absence of all previous history of any rheumatic phenomenon but also by the finding at autopsy of only recent lesions. The streptococcus was not demonstrated in this case. In one patient the first symptoms were those of pulmonary infarct and subsequent pleural effusion, which came on about a month after the termination of a normal pregnancy. In the other case an embolism obliterated the radial pulse.

Fiessinger and Janet²¹ refer to a *rapid* type of this form of endocarditis which the French name slow, malignant endocarditis of the Jaccoud-Osler variety. In one case headache and symptoms of meningeal irritation dominated the picture; there was a suggestive Kernig reaction but no stiffness of the neck; the spinal fluid contained an increase of albumin and a slight increase in lymphocytic cells in the fluid. The duration of this case seemed to be limited to about six weeks. Cultures recovered the streptococcus. At autopsy the characteristic lesions in the heart were found while in the brain only a diffuse congestion with subpial edema could be discovered.

Other reports on this subject have appeared during the past year, but without adding anything to the facts already detailed. There is a striking unanimity in the opinions expressed. Münzer²² states the

¹⁹ Bull. et mém. Soc. méd. d. hôp. de Paris, 1920, xliv, 894.

²⁰ Ibid., p. 910.

²² Zentralbl. f. innere Med., 1920, xli, 282.

²¹ Ibid., p. 1443.

same views and emphasizes that chills and splenic enlargement are signs of very serious significance. Ribiero da Silva²³ echoes the same thoughts.

"PNEUMOCOCCUS TYPE I VEGETATIVE ENDOCARDITIS." This report by Thomas and O'Hara²⁴ is of singular interest. The patient was a white male, aged forty-five years, who was admitted to the hospital three days after the sudden onset of pain in the right side, cough, rusty sputum, bone-aches and vomiting. Physical examination gave evidence of solidification of the entire right lower lobe; this was confirmed by roentgenogram. The leukocyte count was 16,500. Sputum examination and blood culture both were reported, *Pneumococcus* Type I. Treatment with antipneumococcic serum was at once commenced. A week later the temperature was lower and the patient seemed better. Improvement, however, did not continue; the temperature rose again; the physical signs in the lungs showed evidence of early resolution in the lower lobe on each side; the blood culture was found to be still positive; the white blood cell count was 24,000. One day he had a chill. No satisfactory explanation for these continued findings could be discovered and it was suspected that perhaps a pneumococcic endocarditis was present, although no cardiac murmurs were heard at any time. Death took place on the thirtieth day of illness. At autopsy there was found lobar pneumonia of the left and right lower lobes and the lower portion of the right upper lobe. An abscess 4 x 3 x 2 cm. was present in the right lower lobe and a small infarct of the left upper lobe. Bilateral healed pleurisy was present. An acute vegetative endocarditis was present on the tricuspid valve. This process was limited to the tricuspid valve and had given rise at this point to a large vegetative mass of yellowish-gray, slightly friable tissue, over the surface of which there were small pin-point reddish areas. Microscopically the vegetation was composed of masses of fibrin and cellular debris enclosing collections of Gram-positive diplococci. The rest of the endocardium was free from acute lesions, nor was there any chronic endocarditis.

The authors discuss the literature on this subject. Of 141 cases of pneumococcus endocarditis collected by Preble²⁵ in 1904, 12 showed involvement of the tricuspid alone, 56 the aortic alone, 40 the mitral alone and 5 the pulmonary valve alone. The remaining cases showed involvement of more than one valve. Only 18 cases have been reported since 1904. Preble concluded that endocarditis complicates pneumonia in about 1 per cent of all cases and in 5 per cent of fatal cases. In three-fourths of the cases the endocarditis is of a severe or malignant type. *Pneumococcus* endocarditis is much more often left-sided than right-sided, but involvement of the tricuspid and pulmonary valves occurs about four times as often as it does with endocarditis in general. The pneumococcus attacks the aortic valves more often than the mitral and relatively twice as often as the other organisms commonly causing endocarditis. It attacks the tricuspid about twenty times as often as other organisms. The endocarditis may develop before, during or after

²³ Brazil-Medico, 1920, xxxiv, 731.

²⁴ Johns Hopkins Hospital Bulletin, 1920, xxxi, 417.

²⁵ American Journal of the Medical Sciences, 1904, cxxviii, 782.

the pulmonary involvement, but if there is an afebrile period between the fever due to the pneumonia and that due to the endocarditis it is usually only three or four days in length. Physical signs of the endocarditis are often entirely lacking, but its presence should always be suspected in a case of pneumonia which is followed by an irregular temperature not sufficiently accounted for by some other complication such as empyema. The prognosis is extremely grave, for 60 per cent of the cases have a complicating meningitis, but it is probable that the percentage of recovery is higher than the reports published would lead one to infer.

Thomas and O'Hara present the evidence which has accumulated to favor the view that pneumococcus endocarditis is usually caused by the Type I pneumococcus. In the case of endocarditis due to the pneumococcus reported by Tapie and Rouguet²⁶ the whole duration of the final infectious stage was apparently less than two months. A previous valve disease was probable from both history and autopsy findings, but no hint could be obtained as to the steps which led to the pneumococcus infection. The pneumococcus was obtained by blood culture and the autopsy findings were characteristic of a vegetative endocarditis of the aortic and mitral valve leaflets.

Still another similar type of endocarditis is exemplified by the case reported by Blind²⁷ in which the cardiac infection was apparently secondary to suppuration of a war injury. Ten months after amputation of the injured member all the evidences of endocarditis of the aortic and mitral valves were present. At autopsy an ulcerative endocarditis of the mitral and aortic valves was found, with perforation of the left aortic leaflet.

CHRONIC ENDOCARDITIS OR CHRONIC VALVULAR HEART DISEASE. Judging from the available literature on the various aspects of heart disease, interest is shifting from the subject of valvular defects and deformities with their associated murmurs and physical signs and centering more and more on the etiological processes which have brought about the change in the valve, and on the associated myocardial abnormalities on which, in so many instances, the final prognosis depends. Increasing interest is evident in the effects of infections on the myocardium and also in primary origin of these infections which damage the heart. Only a few articles on valvular disease seem worthy of note.

White and Reid²⁸ review the *Diagnosis of Mitral Stenosis*, by which term they mean that deformity of the valve which gives rise to a definite stricture. The diagnosis rests to a great extent on the following points: History of some previous infection of the rheumatic type; history of embolic infarction to the brain or elsewhere, and at times hemoptysis; history of aphonia from paralysis of the left recurrent nerve. On inspection the facies suggest mitral stenosis, the face appearing a little drawn, and there is often a flush, sometimes cyanotic, over the cheek bones. Later an underlying sallowness and more general cyanosis may be

²⁶ Progrès méd., 1920, xxxv, 403.

²⁷ Soc. de méd. de Paris, 1920.

²⁸ Medical Clinics of North America, 1920, iv, 383.

present. The apex-beat exhibits little characteristic to inspection. On palpation a thrill may be found accompanying the apex impulse; it may be systolic, diastolic or both. White and Reid believe the importance of the thrill in mitral stenosis has been overstated. The pulse is not of much diagnostic assistance. Percussion shows the cardiac apex to be in normal position, or if enlargement of the heart is present the border of dulness generally extends laterally rather than downward. Valuable assistance may be obtained by the demonstration of the prominence of the left auricle as a convexity of the curve of cardiac dulness in the left second, third, fourth and fifth interspaces. Auscultation will usually reveal some form or other of the mitral stenotic murmur; it may be a moderately early or mid-diastolic murmur with or without a presystolic phase, or, finally, it may occupy the entire diastolic period except for a brief interval immediately after the second sound. The authors believe that the murmur very rarely occurs solely in late diastole or presystole. When auricular fibrillation is present the presystolic phase of the mitral diastolic murmur disappears and the early and mid-diastolic murmur persists. When cardiac failure is present the murmur is frequently inaudible. In doubtful cases exercise may help to make the murmur more clear. The murmur is heard best over the apex impulse with the bell form of chest-piece, with the patient lying in the left lateral position after exercise. The presence of mitral stenosis is suggested by a sharp and snappy first sound at the apex. In diagnosis the roentgenogram is helpful only in its demonstration of the "mitral-shaped heart in which the organ appears more rounded than normal." The typical electrocardiographic tracing may give evidence of auricular hypertrophy by an auricular or *P* wave over 3 mm. in height or over 0.1 second in duration, and it may also yield evidence of right ventricular preponderance. If these evidences are present we may feel fairly sure of the diagnosis, but the absence of both these changes does not disprove the presence of mitral stenosis. Of course, if the auricles are fibrillating the *P* wave will be absent.

In differential diagnosis White and Reid consider three conditions which may lead to confusion: There is a certain type of normal heart, irritable or excited for some reason, in which a presystolic thrill and a sharp and often reduplicated first sound may be present. These signs are often incorrectly diagnosticated as being due to mitral stenosis. The thyroid heart, on account of its increased force, may resemble this previous group and be confused with mitral stenosis. The auricular fibrillation which occurs both in late cases of thyroid heart and in mitral stenosis further complicates the differentiation. Aortic regurgitation accompanied by the murmur of Austin Flint at the apex gives rise to a most difficult problem of differential diagnosis from organic mitral stenosis. One must look to the accessory signs for assistance.

Concerning the paralysis of the left recurrent laryngeal nerve associated with mitral stenosis, Garland and White²⁹ state that they believe the condition is probably frequently overlooked. This they think

²⁹ Archives of Internal Medicine, 1920, xxvi, 343.

may be due to the fact that the paralysis either is not noted or is not attributed to the underlying cardiac condition. It was formerly believed that the paralysis was due to direct compression of the auricle on the nerve, but the studies of Fetterolf and Norris in 1911 demonstrated that this is practically impossible. Garland and White agree with Fetterolf and Norris that the pulmonary artery must be an intermediate agent in causing pressure, although a thrombus or a mediastinitis may occasionally be the responsible factor. Probably auricular fibrillation is an important additional factor besides the increase in size of the auricle in mitral stenosis, because in auricular fibrillation the auricle remains ballooned out, with the ready production of thrombi. The authors draw one conclusion which to the reviewer appears a little unjustified. They conclude that because the literature contains reports of but 61 cases, not including their own 9 cases, the condition is probably frequently overlooked. It would seem that perhaps the condition is too well known for its incidence or recognition to be judged by the number of cases reported.

Tricuspid stenosis and tricuspid insufficiency are discussed by Young and Cotter³⁰ and four cases are detailed. They emphasize that the symptomatology and physical signs are indefinite and conclude that the most valuable clinical sign of organic tricuspid disease is the presence of a pulsating liver which continues to pulsate, or even pulsates more markedly, under influences calculated to effect the disappearance of this phenomenon.

Pulmonary Regurgitation. Functional insufficiency of the pulmonary valve may develop as a complication of mitral stenosis from two different causes according to Vaquez and Magniel.³¹ In the one instance the pulmonary insufficiency results from mechanical conditions; elevation of pressure in the lesser circulation and subsequent distention of the pulmonary artery and of the valve ring. Under these conditions the prognosis is not made worse by the appearance of the pulmonary insufficiency, indeed, there may be at least a temporary relief of symptoms. In other cases the pulmonary valve becomes involved by an endarteritis of infectious nature and insufficiency results. In these cases the serious prognosis is made even worse by the complication.

Congenital pulmonary regurgitation has been reported recently by Cautley.³² The patient was only a little over two months of age and had been short of breath since birth. Occasionally she had "gone blue," especially after crying. She became more dyspneic and cyanosed for several days, and on the day of death had several attacks of extreme dyspnea and cyanosis. The postmortem examination revealed a large heart with hypertrophied and dilated right auricle and ventricle. The pulmonary artery and orifice were much larger than normal. A transposition of the spleen was also discovered. Apparently the autopsy findings explain the observations made during life that the heart was enlarged and that there was a diastolic murmur heard in the second and third intercostal spaces to the left of the sternum.

³⁰ New York Medical Journal, 1920, cxii, 798.

³¹ Paris méd., 1920, x, 340.

³² British Journal of Children's Diseases, 1920, xvii, 187.

Diseases of the Myocardium. MYOCARDITIS IN INFECTIOUS DISEASES. Comment has already been made on the greater interest which is being shown in affections of the myocardium, and in no field is this more in evidence than in the relation of the various infectious diseases to the myocardium. Diphtheria, scarlet fever and influenza are receiving more attention as causes of myocardial disease, and rheumatic fever is having its influence on the myocardium properly emphasized. Little that is new and that has not been known has been advanced; rather, it is a change in emphasis and point of view.

RHEUMATIC MYOCARDITIS has been carefully studied by Whitman and Eastlake.³³ It will be remembered that in 1916 Aschoff described lesions of the myocardium resulting from rheumatic fever which have been generally accepted as being characteristic of and only produced by this infection. These lesions have borne the name of the "Aschoff body," which the reader has already met in the table of differential diagnosis of rheumatic from other forms of endocarditis. Aschoff believed that these lesions were formed of typical cells which do not arise from muscle cells but are "advential wandering cells." Others have claimed these cells arise from the intramuscular connective-tissue cells of the locality of the lesions.

A typical Aschoff body is "made up of large elements arranged more or less radially about a center, the cells being similar to but larger than the 'epitheloid cells' of a tubercle, more nearly resembling the Sternberg giant cells of Hodgkin's disease. The cells are often multinuclear, with rarely more than six or seven nuclei, and are round, fusiform, or an elongated oval shape. The Aschoff bodies are usually close to small vessels or capillaries and are surrounded by a more or less extensive zone containing chiefly neutrophilic with a few eosinophilic leukocytes, some plasma cells and small lymphocytes." It is agreed by all observers that the Aschoff elements are atypical cells. Whitman and Eastlake studied a case which was considered clearly one of acute rheumatism with cardiac involvement. At autopsy the heart was very large and the pericardium was closely and firmly adherent at all points. The mitral valves were fused, thickened and rigid, but not calcified, with minute vegetations along the edge; the aortic and tricuspid valves were involved in a similar manner. The myocardium showed a large number of typical Aschoff nodules. In the study of these it appeared that it was possible to find all gradations between the Aschoff cell and the muscle cell. In most instances it appeared as though the altered appearance of the muscle cell was the result of degeneration and proliferation of the nuclei. Sometimes the presence of striae at the periphery of the cell suggested that the process at work might be of purely regenerative nature. Whatever the exact process, these authors believe that at least some of the Aschoff cells are derived from muscle cells, and they suggest that the process may commence as a minute infarct. The importance of these lesions depends upon their specificity.

The difficulty of diagnosing myocardial disease initiated during an

³³ Archives of Internal Medicine, 1920, xxvi, 601.

attack of acute rheumatism led Parkinson, Gosse and Gunson³⁴ to review all the available evidence which could be gathered on this point, in a series of 50 cases of acute rheumatic fever. They attempted to find signs indicative of an acute myocarditis or myocardial disease which might be likely to eventuate in heart failure. They interested themselves especially in the size of the heart and its disturbances in rate and rhythm. Murmurs were also observed, but proved of little value in the question under consideration. Their summary in part is as follows:

"The size of the heart, as indicated by the position of the apex-beat, varied little. A change exceeding one-half of an inch was only noted in 6 of the 35 cases where the apex was palpable. Of the 35 cases, the heart increased in size in 10, decreased in 10, increased then decreased in 3 and remained unchanged in 12. The enlarged heart discovered in acute rheumatism often depends upon a complication or proves to be a sequel of a previous attack. The frequency and degree of enlargement of the heart during an attack of acute rheumatism have been exaggerated, and the enlargement is usually slight when it does occur.

"No definite relationship was found between the development of systolic murmurs at the apex and apparent enlargement of the heart. Thus in only one of the 5 cases in which a systolic murmur actually developed under observation was any increase in size recorded.

"Sinus arrhythmia was present after the attack in 47 of the 50 cases (94 per cent). It was demonstrated in 2 cases with a pericardial rub, 1 case with a pericardial effusion, 1 after auricular flutter and in each of the 15 cases which had developed acute heart-block. The presence of sinus arrhythmia does not indicate that the heart has escaped infection.

"Premature auricular contractions appeared in 7 cases (14 per cent); two types are distinguished. A paroxysm of auricular flutter was recorded in 1 of these cases. An irregularity observed from time to time in 3 cases is interpreted as ventricular automatism rather than nodal rhythm.

"Auricular disease, such as fibrillation and flutter, is often the sequel to acute rheumatism; the frequency of auricular premature contractions in this infection and their association with flutter and with heart-block suggest that they indicate acute myocarditis.

"Acute heart-block (*a-v*) developed in 15 of the 50 cases (30 per cent), proceeding to the degree of dropped beats in 4 (8 per cent). It often appeared quietly in the absence of other signs such as pyrexia and tachycardia, and it invariably disappeared during convalescence.

"The authors conclude that acute heart-block of some grade is common in acute rheumatism; that it indicates acute myocarditis, and that it may therefore be premonitory of chronic myocarditis and eventual heart failure."

It must be noted that the authors include delayed conduction time under the term heart-block, and while it is true that a lengthened *a-v*

³⁴ Quarterly Journal of Medicine, 1920, xiii, 363.

interval is the first stage of heart-block, yet by many the term heart-block is limited in its meaning to include only those cases in which dropped beats or some definite alteration of the normal 1-1 relation of ventricular to auricular contraction are found. Of the 4 cases which showed heart-block of this degree, 3 showed only dropped beats and in 1 case a 2-1 heart-block was present.

This interesting study carries weight not only because of the standing of its authors, but also because of its detail and thoroughness. It is important for us to appreciate the frequency of disturbances of rhythm in acute rheumatic fever and to be on the watch for them, as it is possible that they will prove to be of prognostic import in regard to cardiac function in later life.

POSTINFLUENZAL AFFECTIONS OF THE MYOCARDIUM have been considerably discussed since the recent epidemics. Necropsy studies have revealed in many instances acute parenchymatous changes in the myocardium. This opinion is not unanimous and some conflict in opinion still exists. Hamburger,³⁵ however, believes that opinion is beginning to crystallize as follows:

1. Necropsies of fatal cases of influenza, in spite of slight gross pathological changes in the heart, show rather universally acute parenchymatous degeneration and vacuolization, and, at times, extensive myocardial damage.

2. Clinical studies during the acute stage of illness and in convalescence indicate a rather remarkable recoverability of complete cardiac function. The postinfluenzal flabby heart muscles gradually disappears under graduated and properly directed exercise.

3. Certain of these acute myocardial processes, however, do not clear up, at any rate for a very long time, and become cases of true postinfluenzal myocardial insufficiency.

Hamburger reports 6 cases as examples from a larger group in evidence that the acute epidemic respiratory infections known as influenza cause damage to the cardiac mechanism which may be demonstrated clinically and electrocardiographically. By this latter method it is shown that these infections affect, for the most part, the auricle and the conduction pathways of the heart. Possibly it is the streptococcus which thus singles out early the auricle and the conduction pathways. Possibly the ventricles are similarly affected, but are slower, for structural reasons, to give evidences of the involvement. In the non-fatal acute cases there occurs, as a rule, complete restoration of the cardiac mechanism to normal within a period of from two to six weeks.

In 5 of the cases reported by Hamburger there was present either heart-block, auricular extrasystoles or both. Similarly, Cockayne and also Barker have published, in 1919, evidence showing the tendency in these cases to involvement of the auricle and of the bundle of His. Bard whose article on bradycardia was mentioned last year explained the slow pulse of convalescents from influenza, etc., as being due to premature auricular extrasystoles. This is denied by De Meyer,³⁶ who

³⁵ American Journal of the Medical Sciences, 1920, clx, 479.

³⁶ Arch. d. mal. d. cœur, etc., 1920, xiii, 300.

interprets otherwise Bard's own tracings. De Meyer also states that the convalescent with bradycardia presents no cardiac distress nor palpitation, and this is a strong argument against there being an extrasystolic arrhythmia present. Although isolated extrasystoles may induce no discomfort, yet repeated extrasystoles, he claims, always lead to palpitation and cardiac complaints. Hamburger's cases, it may be stated, had definite cardiac complaints and symptoms.

DIPHTHERIA has a very profound influence on the myocardium, as was pointed out last year in this review. Further evidence has been presented by McCulloch.³⁷ From a group of 80 cases of diphtheria, 19 showed evidence of cardiac disturbance and all 19 died. It is the heart muscle which is especially involved, and evidence of the disease is presented by the disturbance in the cardiac mechanism. Myocarditis due to diphtheria has a definite position among those factors that lead to chronic heart disease later in life. Allen³⁸ has reported an instance of complete heart-block developing on the seventh day of an attack of diphtheria. The patient, a girl, aged seventeen years, was apparently doing well, when she had a sudden convulsion with marked cyanosis; the pulse became imperceptible, and on return was found to be only twenty-six per minute. It was thought that muffled auricular sounds could be heard—fifty-two per minute, while the ventricular rate was twenty-six per minute. Two further convulsions during the following two days preceded her death.

TYPHOID FEVER is well known to affect the heart muscle. Pezzi and Silingardi,³⁹ in an article published some two years ago, report on a study of the heart in typhoid and paratyphoid fevers and attempt to differentiate the involvement in the two, without, however, much success. They comment on the infrequency of disorders of conduction; 1 case of typhoid exhibited a partial block, and extrasystoles were present in 5 per cent of the cases. The authors feel that typhoidal myocarditis is a difficult diagnosis and one which must be made with prudence; endocardial or pericardial complications of typhoid fever they have never seen.

MALARIA also may bring about myocardial degeneration. In an interesting article on malignant malaria in Macedonia, Gaskell and Millar⁴⁰ give a description and a drawing of the acute degeneration and fragmentation of the heart muscle fibers which take place in the so-called "septicemic" type of malignant malaria. They also recognize a "cardiac" type in which chronic degeneration of the heart muscle ultimately leads to cardiac decompensation which dominates the picture and overshadows the causative infection.

SYPHILIS of the heart muscle is too well known to require more than mention. Certain cases of sudden death from cardiac disease have already been reviewed in this article, and it may be noted that sudden death from rupture of the heart is usually due to gumma of the myo-

³⁷ American Journal of the Diseases of Children, 1920, xx, 87.

³⁸ British Medical Journal, 1921, i, 267.

³⁹ Le Malattie del Cuore, 1919, No. 12, p. 369.

⁴⁰ Quarterly Journal of Medicine, 1920, xiii, 381.

cardium and permanent slow pulse to syphilitic lesions of the bundle of His. Oddo and Mattei⁴¹ remind us that even secondary syphilis may bring about a cardiac death. It is usually the vessels and the pericardium which syphilis attacks, but also the myocardium, although the symptoms of this latter trouble may be mild and indefinite. Later, however, in life the myocardial changes may become important. Most authorities will not go as far as does Gaucher, who is quoted by Oddo Mattei as having said in 1917 that fibrous myocardial hypertrophy and the interstitial nephritis which it accompanies are both, in the majority of cases, produced by syphilis.

SCARLET FEVER. The heart in scarlet fever is reported on by Rosenbaum⁴² as a result of a study of 1770 patients with scarlet fever. Of this number, 106 exhibited cardiac complications. An analysis of this group of 106 cases revealed that 12 had valvular defects antedating the scarlet fever; in the remaining 94 cases a diagnosis of myocarditis was made in 88, of endocarditis in 4 and pericarditis in 3. This group does not include the many cases which showed merely an increased rapidity or an occasional slight irregularity. The cases of myocarditis were classified as mild, moderately severe and severe. Mild cases, of which there were 53, were those with persistent feebleness, rapidity or irregularity of pulse, but with little other disturbance. Four cases in this "mild" group died, but of causes not related directly to the heart. Thirty cases of myocarditis were moderately severe, with a higher grade of myocardial disturbance, sometimes with definite signs of cardiac dilatation. All of this group recovered. The severe cases were those in which the cardiac disturbances were so severe as to render the prognosis very doubtful. They were characterized by signs of cardiac dilatation, cyanosis and marked irregularity, feebleness and variations in the pulse-rate. Five cases were in this group, 1 of whom died, possibly of cardiac disease.

It is interesting to note that myocarditis was observed more frequently in the early years of life. It may occur at any time in the course of the illness, but is commonest in the latter days of the acute state or in early convalescence. The presence of other complications, as might be expected, seems to increase the incidence of myocarditis. Although it has been suggested that the tachycardia of scarlet fever may be the result of the direct action of the virus on the nervous mechanism of the heart, yet there is sufficient evidence that changes in the heart muscle are frequent in scarlet fever. Perhaps in short cases the cause of the heart weakness lies in pathological changes in the heart ganglia, but there is quite constantly, in even mild cases, some parenchymatous change in the heart muscle, while in more severe or prolonged cases fatty degeneration and necrosis may be added. Some have believed that pericarditis was the characteristic heart lesion of scarlet fever, and others have reported endocarditis as occurring quite frequently. The series reported by Rosenbaum lends no support to these views; it is true, however, as Rosenbaum points out that this may be due to the

⁴¹ Arch. d. mal. d. cœur, etc., 1920, xiii, 19.

⁴² Archives of Internal Medicine, 1920, xxvi, 424.

milder type of scarlet fever with which he was dealing. The case mortality in his series was less than 4 per cent.

P. D. White, in a recent address on the heart in infectious diseases, pointed out that the so-called "effort syndrome" often appears during, or shortly following, an acute infection and that the symptoms resulting from this effort syndrome are often incorrectly attributed to true cardiac disease. There are few symptoms of general injury to the heart in infectious diseases. Ready dyspnea and fatigue are often not due to true damage of the myocardium; early in an infection they may result from the toxemia, late from exhaustion. Undoubtedly true damage does occur, but it may not always be what it appears. For example, acute dilatation may in fact be a rapidly developing pericardial effusion. White, in referring to the therapy of the heart in acute infection places the specific treatment of the infection first, good nursing second and symptomatic drug treatment last. In diphtheria and syphilis we have specific remedies, and, by the way, every syphilitic should be examined for heart involvement. In rheumatism, salicylates and tonsillectomy are almost specific. It is probable, he suggests, that stimulants, including digitalis, may be wasted in infectious diseases unless there is a chronic cardiac involvement present.

Size of the Heart. Closely related to the question of myocardial disease is that of cardiac size and cardiac dilatation. Much that is confusing and contradictory has been written on this subject. Kaufmann⁴³ reports on the roentgenographic examination of 70,000 men with heart symptoms. Many of these men had abnormally enlarged hearts, but in the majority the heart was structurally sound. Almost all these men were soldiers and were undergoing various degrees of physical exertion. The dilatation of the heart which was found in so many of them was analogous to the dilatation which Kaufmann believes occurs with excessive athletic strain. Certain factors tend to such dilatation, for example, preceding infectious disease or overstrain in the untrained. Some such factor was present in 85 men with long-continued dilatation; in only 15, however, did the condition progress to actual insufficiency of the myocardium. A history of one of the infectious diseases which are known to affect the myocardium and a finding of cardiac dilatation justifies a diagnosis of chronic myocarditis. This, however, may merely indicate that the heart is not quite up to par, although structurally unaffected. Apparently it is the authors' desire to emphasize the importance of previous infectious disease as a factor in the later development under strain of an enlargement of the heart. That this enlargement is dilatation he seems to assume on what appears to be insufficient evidence.

Cohn⁴⁴ investigated the size of the heart in soldiers by the teleroengen method, with the plate six feet from the roentgen ray-tube. Soldiers who had seen active service in the A. E. F. were chosen for this study; 208 soldiers were studied, but of this number 47 had suffered from an acute infectious disease, and these 47 were therefore discarded. As a

⁴³ Wien. Arch. f. inn. Med., 1920, i, 211.

⁴⁴ Archives of Internal Medicine, 1920, xxv, 499.

result of his studies, which were exceptionally carefully carried out, Cohn comes to the following conclusions:

1. In normal breathing the difference in the size of the heart during inspiration and expiration may be neglected.
2. The use of the transverse diameter of the heart shadow is a satisfactory measurement. It is as useful as and less uncertain than the long diameter or the area.
3. The range of the observed measurements interferes with the usefulness for the clinic of standard and average curves.
4. The hearts of soldiers examined under conditions stated are not larger than those of normal individuals.

Smith⁴⁵ carried out similar investigations on 277 men selected from the orthopedic service who had had active fighting service overseas. Only those men were selected for this study who had been free from cardiac symptoms during their period of military service and who had had no infectious disease since entering the army. These were also studied by the teleroentgen method. In this study no evidence was found that the hearts of soldiers are enlarged after active military service. Smith does not entirely agree with Cohn and believes there is danger in basing an opinion of size on the determination of the transverse diameter alone.

Smith⁴⁶ also studied in the same manner cases of effort syndrome in which symptoms had persisted for a long time and found that such men have smaller hearts than normal when compared by measurements of the transverse diameter, area and volume. These small hearts varied as widely in form as do normal hearts, and the narrow, long heart or "drop heart" was not found to be the predominant type. It was found, however, that the hearts with smaller measurements were found in those men whose skeletal musculature had never been developed normally.

Angina Pectoris. It is difficult for the reviewer to decide under what heading to place the few notes available from current literature concerning angina pectoris. Heberden, the first observer of angina pectoris, did not regard it as a symptom of heart disease at all, although he considered it spasmodic rather than inflammatory. For many years it was accepted as true that angina pectoris was a symptom resulting from disease of the coronary arteries. In 1915, Allbutt completely denied the coronary hypothesis and expressed views which led to a still unsettled controversy. Repeated attempts have been made in older days to locate the disease in the nervous system, but of recent times it has been generally located in the heart—but whether this symptom results from disease of the myocardium, aorta or coronary artery is far from agreed upon.

On July 21, 1768, Heberden⁴⁷ presented before the College of Physicians in London "Some Account of a Disorder of the Breast." His short account includes the following: "There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind

⁴⁵ Archives of Internal Medicine, 1920, xxv, p. 522.

⁴⁶ Ibid., p. 532.

⁴⁷ Medical Transactions of the College of Physicians, London, 1772, ii, 59.

of danger belonging to it, and not extremely rare, of which I do not recollect any mention among medical authors. The seat of it, and sense of strangling and anxiety with which it is attended, may make it not improperly be called *Angina pectoris*."

"The *os sterni* is usually pointed to as the seat of this malady, but it seems sometimes as if it was under the lower part of it, and at other times under the middle or upper part, but always inclining more to the left side, and sometimes there is joined with it a pain about the middle of the left arm. What the particular mischief is, which is referred to these different parts of the sternum, it is not easy to guess, and I have had no opportunity of knowing with certainty. It may be a strong cramp, or an ulcer, or possibly both.

"The pulse is, at least sometimes, not disturbed by this pain, and consequently the heart is not affected by it; which I have had an opportunity of knowing by feeling the pulse, during the paroxysm; but I have never had it in my power to see any one opened, who had died of it; the sudden death of the patients adding so much to the common difficulties of making such an inquiry, that most of those with whose cases I had been acquainted, were buried, before I had heard that they were dead."

Within a short time after the publication of this description of *angina pectoris*, Heberden⁴⁸ received a letter from an anonymous writer stating that he, the writer, suffered from the condition which Heberden had described, and further stating: "I have left directions on my will to send an account of my death to you, with a permission for you to order such an examination of my body, as will show the cause of it; and, perhaps, tend at the same time to a discovery of the origin of that disorder, which is the subject of this letter, and be productive of means to counteract and remove it." In less than three weeks after receiving this letter, Heberden was notified that the anonymous writer had died. Heberden procured "that experienced and accurate anatomist, Mr. J. Hunter to open the body. . . ." "In general, the viscera were well formed and in a sound state, with marks of great robustness. The contents of the thorax were examined with peculiar attention, particularly the heart with its vessels and valves, and were all found to be in a natural condition, except some specks of a beginning ossification upon the aorta, and some adhesions of the lungs to the pleura on the left side. The left ventricle of the heart was remarkably strong and thick, and as perfectly empty of blood, as it if had been washed." "This anatomical examination, for which I acknowledge myself much indebted to the manly sense and benevolent spirit of this worthy man, though it does not inform us, what the cause of the disease was, will, however, have its use by informing us what it was not."

It is interesting to read these notes, written one hundred and fifty years ago, and to appreciate the clearness of the clinical description of the disease, even though it is probable, with the causative pathology before their eyes, its significance was not recognized. It would seem

⁴⁸ Medical Transactions of the College of Physicians, London, 1785, iii, 1.

that we have not, perhaps, advanced so much further in this matter during the past century and a half.

Willius⁴⁹ reports an electrocardiographic study of angina pectoris. He undertook a critical study of 155 cases, including a careful analysis of clinical histories, physical findings, electrocardiograms and other adjunct laboratory data. Nineteen patients (12.2 per cent) had recognizable aortic lesions, 4 of which were of syphilitic origin. Seven patients had aortitis, 4 aortic regurgitation, 5 aortitis and aortic regurgitation, 2 aortic stenosis and 1 patient had an aneurysm of the descending aorta. Seven patients having syphilis did not have clinical evidence of aortic disease, although the heart was invaded by disease. In this group the possibility of unrecognized aortitis producing atresia of the coronary orifices must be considered, although this type of aortitis is usually recognized. Two patients (1.3 per cent) had mitral stenosis.

The remaining 134 patients (86.5 per cent) had indeterminate pathological lesions if coronary disease be left out of consideration, as Allbutt's work would suggest. Willius states that he finds it difficult to classify this large group of patients (86.5 per cent) if coronary disease is not responsible for their angina. If aortic disease were present it was not detected clinically, and such a high percentage of diagnostic error is certainly unlikely. No instance of adhesive pericarditis was noted.

The series comprised 128 males and 27 females. The greater number of patients were found in the fifth (34), sixth (59) and seventh (45) decades. Seven patients (4.6 per cent) did not have objective evidence of heart disease.

The following table is made up to show the incidence of various electrocardiographic abnormalities in this series and the mortality in each group. Thirty electrocardiograms (19.4 per cent) were considered normal.

Electrocardiographic findings.	Number of cases.	Percentages.	Mortality:		
			Heard from.	Died.	Percentage.
Changes in final ventricular T-wave	18	11.6			
Significant T-wave negativity	51	32.9	37	26	70.3
Abnormal Q R S in all leads	22	14.2	16	10	62.5
Abnormal Complexes in isolated leads	33	21.2	47.3
Abnormal Complexes slurred	26	16.7	20.0
Delayed a-v conduction	2	1.3	1	1	
Complete heart-block	1	0.6	1	1	
Auricular fibrillation	3	1.9	2	2	

The cardiac mortality of the complete group was 46.7 per cent definitely contrasted by the higher mortality attending those patients having significant T wave negativity and abnormal Q R S complexes in all derivations (leads) of their electrocardiograms. Willius concludes there are no electrocardiographic findings pathognomonic of angina pectoris. The high percentage of cases in this series in which electrocardiographic evidence of myocardial disease was present is instructive, but, of course, not conclusive.

⁴⁹ Archives of Internal Medicine, 1921, xxvii, 192.

Angina pectoris in diabetics is emphasized by Kahn⁵⁰ as being quite common and not sufficiently well recognized. Diabetes, he states, is essentially a disease of low blood-pressure unless a complicating cardio-renal trouble is present. Too often the diabetic is assumed to have a high pressure and is treated with the various drugs that induce reduction of blood-pressure in an attempt to ameliorate the pain of angina pectoris. Kahn believes that these anginal attacks do not occur when the patient's glucose tolerance is not exceeded. A high blood sugar with glycosuria in such an individual will frequently cause the recurrence of the painful attacks. He also comments on the frequency with which diabetic patients suffering from angina pectoris will show an inversion of the *T* wave in one or more of the three leads of the electrocardiogram.

ANGINA PECTORIS AND AURICULAR FIBRILLATION. It has often been said that angina pectoris does not appear in cases with auricular fibrillation, and that, in fact, a patient who has had attacks of anginal pain may be relieved and become free of attacks if auricular fibrillation develops. That this is not the invariable rule is evident from such a case as that reported by Sandison.⁵¹ The patient was a woman, aged seventy-two years, who for many years had suffered from cardiac trouble, with occasional periods of slight decompensation. A more serious breakdown associated with breathlessness on exertion, palpitation, frontal and occipital headaches, was also characterized by attacks of undoubted angina pectoris. The pain was paroxysmal, of varying severity, and situated in the region of the heart; it was sudden in onset and associated with a feeling of tightness in the front of the chest, mental perturbation, intense anxiety and a sense of numbness in the left arm. At this same period the pulse was completely irregular, with a ventricular rate of 124 per minute. The blood-pressure in systole was 210 mm. A diagnosis of auricular fibrillation and true angina pectoris was made by Sandison, and this was confirmed by F. W. Price in consultation. In 1917, Price, in his book *Diseases of the Heart*, stated that "it would appear, however, that patients suffering from auricular fibrillation are exempt from definite attacks of angina pectoris." In a footnote to Sandison's report, however, Price states that since 1917 he has observed 2 previous cases of auricular fibrillation (proved by electrocardiographic examination) who also suffered from typical attacks of angina pectoris.

Pinheiro⁵² admits that the prognosis in angina pectoris is extremely serious, but advises that one should be cautious in giving this prognosis. It is sometimes difficult to be certain of the diagnosis, and it is no trivial matter to give an extremely grave prognosis to a patient who has nothing more seriously wrong than a neurosis or is a habitual air-swallower with resulting symptoms which suggest angina pectoris.

Jonnesco⁵³ has tried the total resection of the cervical sympathetic, including the first thoracic ganglion for the relief of angina pectoris.

⁵⁰ Journal of the American Medical Association, 1921, lxxvi, 570.

⁵¹ British Medical Journal, 1921, i, 339.

⁵² Brazil-med., 1920, xxxiv, 151.

⁵³ Ibid., p. 93.

This was attempted on the assumption that the symptoms of angina pectoris are the result of reflex action of irritation of the cardio-aortic plexus, and that by cutting on the left side the communication between this plexus and the nerve centers the reflex arc might be broken and relief obtained. The patient in whom this operation was performed was a man, aged thirty-eight years, syphilitic and an excessive user of alcohol and tobacco. In four months the patient had five characteristic and severe attacks of angina pectoris, and enlargement of the aorta and heart could be demonstrated. Since the operation four years ago there has been no further attack, not even of the mildest nature. The patient expressed great gratitude even though some asymmetry of the face developed as a result of the falling back of the left eyeball; also, the left pupil became somewhat contracted.

Disease of the Pericardium. None of the literature published during the past year on the subject of the pericardium equals in interest the work reviewed last year in this article. A case which well exemplifies the tremendous EFFECT WHICH PERICARDIAL EFFUSION MAY HAVE ON THE CIRCULATION has been recently reported by Freese.⁵⁴ The patient was stabbed and the wound traversed the pericardium and both ventricles of the heart. When seen at the hospital, about three-quarters of an hour after the injury, no pulse was perceptible in the radial or the carotid arteries. At the operation the reason for the lack of pulse was apparent, as the pericardium was filled by blood-clot which produced almost a complete tamponade. When this clot was scooped out the heart began at once to beat violently and soon a pulse could be felt by the anesthetist. Recovery followed the operation, although the patient's condition at the end of the operation was precarious and the heart had almost stopped beating. It is in this same manner that recent rapidly forming pericardial effusions bring about circulatory distress at a time before the pericardial sac has dilated. Early a small effusion may be dangerous, while later the distended pericardial sac may accommodate a large effusion with few or no symptoms.

Involvement of the pericardium incident to diseases other than true inflammation of the pericardium is far more common than is generally appreciated. In some such instances the name "pericarditis" is perhaps employed without justification, although this is a matter of opinion; for example the well-known occurrence of pericardial frictions in the course of a chronic nephritis, usually of the glomerular variety. An example is furnished by the case reported by Chauffard and Huber.⁵⁵ Their patient became uremic following the termination of a pregnancy and the pericardial complication appeared about a week later. Later all evidence of the pericardial friction disappeared, but the woman died of the kidney disease about three months later. At the autopsy the pericardial cavity contained no excess of fluid, but all over the surface of the right ventricle and auricle there was present a light fibrinous deposit of an opalescent, whitish appearance. Histologically, the visceral pericardium was found to be irregularly thickened, without

⁵⁴ Journal of the American Medical Association, 1921, lxxvi, 520.

⁵⁵ Bull. et mém. Soc. méd. d. hôp. de Paris, 1921, xlv, 101.

any trace of recent lesions. The underlying myocardium was almost normal, but in occasional small vessels bacterial thrombi composed of cocci and diplococci could be seen, although there were no lesions of the heart valves. Pericarditis as a complication or coincident feature of coronary thrombosis is also well known. Sternberg has proposed the name "pericarditis epistenocardia" for a symptom-complex consisting of stenocardia (angina pectoris), fever, pericarditis and some degree of myocardial insufficiency. Gorham⁵⁶ has reviewed the literature on this subject and reports 6 cases with autopsy in 3. From these cases he concludes that the condition is probably often overlooked and that pericardial friction is the most important and characteristic single sign of the syndrome. The difficulty in detecting the friction rub, because of its light quality, its sharply defined localization, and its transitory or recurrent character, is to be especially emphasized. In some instances the knowledge of this syndrome makes possible the diagnosis of coronary thrombosis during life in a certain number of cases, and may even lead to a tentative diagnosis of aneurysm of the heart in certain instances. It must be apparent that this group of cases of pericarditis must come close in certain instances to the preceding.

Cunnington⁵⁷ claims to have observed an acutely developed pericardial effusion following the administration of antidiaphtheric serum in the course of a mild case of diphtheria. While the signs of the effusion seem to have been clear the relation of its development to the serum seems doubtful or at least unproved. The subsequent course of the case was uneventful and recovery was complete.

LIPOMA OF THE PERICARDIUM is reported by Allalouf and Bernard.⁵⁸ The finding was at autopsy on an obese, plethoric woman, aged seventy-four years, who had died of cerebral hemorrhage. Apparently the lipoma, which measured 10 x 6 x 1 cm., had not interfered with the circulation in any way. Such a finding is not frequent, but, on the other hand, is not extremely rare.

CHRONIC ADHESIVE PERICARDITIS. A study of the conditions in association with which chronic pericardial adhesions are found at autopsy was undertaken by Lyter.⁵⁹ Of 514 patients coming to autopsy consecutively, 1.5 per cent (8 cases) had extensive pericardial adhesions, 3.5 per cent (18 cases) had moderate adhesions and 0.8 per cent (4 cases) had mild adhesions. The apparent causes of death in the three groups were as follows:

In the cases with extensive adhesions: Typhoid fever, 3 cases; acute endocarditis, operation for adhesions, carcinoma of the stomach, each 1 case; chronic nephritis, 2 cases.

In the cases with moderate adhesions: Cerebral apoplexy, 2 cases; carcinoma of the liver, carcinoma of the stomach, pulmonary tuberculosis, each 1 case; acute nephritis, 11 cases.

In the cases with mild adhesions, 2 died of cirrhosis of the liver and 2 from chronic nephritis.

⁵⁶ Albany Medical Annals, 1920, xli, 109.

⁵⁸ Jour. de méd. de Bordeaux, 1920, xci, 516.

⁵⁹ American Journal of the Medical Sciences, 1920, clxx, 891.

⁵⁷ Lancet, 1920, i, 1009.

It is interesting to note that 50 per cent of the series died from nephritis, and in the entire series only one heart was found without marked changes in the myocardium, the endocardium or in the large vessels. Apparently a large number of instances of pericardial adhesions fail to fall in the group due to tuberculosis and to attacks of acute pericarditis in acute infectious diseases such as rheumatic fever, tonsillitis, lobar pneumonia, typhoid, etc. This other group gives no history of previous infections of any kind and the adhesions are probably the result of long or continued injury to the pericardium from chronic infections or some unknown intoxication; in this class we see most typically the associated chronic changes in the liver and kidneys. In this class the formation of the adhesions is insidious, only resulting in cardiac symptoms years later. Unless the adhesions are selectively located or are very extensive the clinical recognition is not only impossible but unimportant.

Lyter emphasizes the importance of inspection in the diagnosis during life of pericardial adhesions. Palpation and auscultation are of little help, but on inspection one may often see a distinct retraction of the lower end of the sternum and the costal cartilages synchronous with cardiac systole. Well-defined cardiac decompensation, without valvular or myocardial changes to account for the decompensation, should always arouse suspicion of adherent pericarditis.

Gil-Casares⁶⁰ suggests that the coexistence of pleurisy with pericarditis is common and that the initial acute phase of the pericarditis may be overshadowed by the signs and symptoms of the pleurisy. Rehn⁶¹ believes that many cases of adhesive pericarditis in children are overlooked. He operated on 4 cases with some temporary improvement, but it must be remembered that in childhood pericarditis is usually a part of a pancarditis or is tubercular in nature. In either case the adhesions in the pericardium are only one feature of the disease and little can be hoped from the surgical relief of the adhesions.

We cannot be reminded too often of the frequent occurrence of acute abdominal symptoms from supradiaphragmatic disease. The well-known simulation of acute appendicitis by an early basal pneumonia on the right side is a good example and the abdominal pain in angina pectoris is another. Pericarditis with abdominal symptoms is described in 3 cases by Holden.⁶² In all 3 laparotomy was performed before the correct diagnosis was made. In one perforating ulcer, in another appendicitis and in the third some acute abdominal trouble was suspected. The abdomen was found normal in all 3 and the later discovery of the cardiac trouble made the correct diagnosis clear.

Congenital Deformities of the Heart. CHIARI'S NET. Parkes Weber⁶³ has reported 2 interesting cases in which a so-called Chiari's net was found in the right auricle of the heart, with or without the presence of any other congenital cardiac abnormality. This "net" is the abnormally persistent remnant of a normal structure in the right auricle of

⁶⁰ *Siglo méd.*, 1920, lxxvii, 837 (abstract, *Journal of the American Medical Association*).

⁶¹ *Archiv f. Kinderheil.*, 1920, lxxviii, 179.

⁶² *Northwest Medicine*, 1920, xix, 230.

⁶³ *International Clinics*, 1920, iii, 43.

the human fetal heart. It is a vestigial remnant of the fetal *septum spurium*, namely, the portion of it constituting the *valvula venosa dextra*. It is found attached to the Eustachian valve, and, by one or more threads, to the heart wall in the region of the *tuberculum Loweri* and the *crista terminalis*. It cannot be diagnosticated during life and is very seldom observed at postmortem examination, but doubtless would be oftener found if methodically and regularly looked for. It is liable to be associated with other congenital cardiac abnormalities, and, though very rarely, thrombi may form on the net during life and give rise to pulmonary embolism. This accident occurred in Chiari's first case and in a case described by Looser in 1920.

The first case described by Weber was one of congenital disease of the right side of the heart affecting the pulmonary and probably also the tricuspid orifices. In addition a malignant endocarditis had supervened on the tricuspid valve and had involved also the pulmonary artery. Chiari's net was found in the right auricle. In the second case the net in the right auricle was found at the postmortem examination, unaccompanied by any other cardiac abnormality. Death had occurred from sarcoma, probably originating primarily from the kidney.

A most unique case of congenital deformity of the heart was reported before the Section of Medicine of the Royal Society of Medicine by Professor Arthur Keith and MacDonnell⁶⁴ under the title: "Case of Transposition of the Viscera showing a Potentially BICAMERAL HEART." The little girl, aged seven months, suffered from slight cyanosis and dyspnea and died from an exacerbation of these symptoms and cough. There was no clubbing of the fingers, but a large liver was in evidence. During life it had been recognized that the heart was on the right side, and it was suggested that there was congenital deformity of the heart as well. Keith reported that at autopsy "the heart was on the right, the liver on the left, the spleen on the right; the stomach, small and large bowel, the kidneys, adrenals, arteries and veins all lying as in a mirrored image of the normal disposition." The great veins were also affected; the inferior vena cava and the superior vena cava entered a systemic auricle. The auricles were transposed and the pulmonary veins did not enter the pulmonary auricle but the systemic. The ventricular chambers, however, were not transposed, although there had been transposition of the aortic stems in relation to their respective ventricles. Apparently the only blood which reached the systemic circulation did so through a patent ductus arteriosus from the "pulmonary aorta," into which blood was pumped by what would normally be the left ventricle. The other ventricle from which the systemic aorta opened was in reality a "dummy pump." In brief: "All the blood from the lungs and from the body was received in one chamber of the heart—the systemic (normal right) auricle. From that auricle it entered the left ventricle, and that chamber served as a pulmonary and systemic pump, the only blood reaching the systemic circulation being that which passed into the aorta by a constricted ductus arteriosus. The two

⁶⁴ Proceedings of the Royal Society of Medicine, Sect. of Medicine, January, 1921; xiv, 1.

other chambers of the heart, the pulmonary auricle and right ventricle, although fully developed, appear to have taken no part in carrying on the circulation."

In an extraordinary case of total situs inversus of the viscera, reported by Lineback,⁶⁵ special interest is attached to the state of the heart. This organ showed remarkable abnormalities; it was completely reversed, and, in addition, showed several anomalies which justified the belief that the heart was in an early embryonic state of development. This is of importance in view of the fully developed body with which this heart was associated. From this fact the author concludes that the causative factor in the production of such anomalies operates at a very early embryonic period. This is contrary to the opinion expressed by some writers who attribute such malformations to trauma in late embryonic life.

CONGENITAL MALFORMATION OF THE MITRAL VALVE is reported by Castelli.⁶⁶ The patient died of cancer of the stomach at the age of sixty-five years and the cardiac anomaly was found at necropsy. On examining the heart the left ventricle was thickened and there was slight deformity of the aortic cusps. The chief deformity concerned the mitral valve; its aortic and lateral cusps were partly inserted to the upper part of the interventricular septum, which presented an aneurysmal dilatation toward the right ventricle. Throughout life there had been no evidence of disturbance of circulation. The author refers to seventeen similar cases which he has found in the literature.

DEXTROCARDIA FROM MEGACOLON. In this review last year considerable space was devoted to the subject of dextrocardia, but one case reported this past year is worthy of mention. It is reported by Carnot and Friedel.⁶⁷ A man, aged fifty-five years, had a very large colon which pushed the heart over to the right and also displaced the stomach, spleen and liver. Resection of the enlarged splenic flexure of the colon allowed the displaced organs to resume their normal positions. Unfortunately the change of position of the heart so affected the circulation as to result in fatal collapse the day after the operation. This is the authors' explanation for the patient's death, and they suggest that if by packing the heart had been kept from too rapidly resuming its usual position the result might have been more favorable.

Syphilis of the Heart. St. George⁶⁸ reports 2 cases; 1 of rupture of the heart from a gumma situated on the anterior surface of the left ventricle near the apex and 1 of spontaneous rupture of the aorta. In neither case was any history obtainable. It is probable that both patients had syphilis, but there was no apparent aneurysm or gumma of the aorta. In fact the cause of the rupture of the vessel is in doubt. Luce⁶⁹ emphasized the importance of diagnosing syphilitic disease of the heart in individuals with cardiac trouble and a positive serological test, especially if there is an absence of other etiological factors. The

⁶⁵ *Journal of the American Medical Association*, 1920, lxxv, 1775.

⁶⁶ *Il Morgagni*, 1920, lxii, Arch., 376.

⁶⁷ *Arch. d. mal. d. l'appar. Digestif.*, 1920, x, 577.

⁶⁸ *American Journal of Syphilis*, 1920, iv, 702.

⁶⁹ *Deutsch. med. Wchnschr.*, 1920, xlii, 66.

spontaneous rupture of a gumma of the interventricular septum, with the resulting physical signs and symptoms, may suggest the diagnosis. He is pessimistic concerning the ultimate successfulness of antispecific treatment because of the obliterating endarteritis which is so often an accompaniment of any type of cardiac syphilis.

RUPTURE OF A PAPILLARY MUSCLE. A case with this unusual finding is reported by Spalding and von Glahn.⁷⁰ The patient was a colored male, aged thirty-one years, who after a period of over a year of increasing decompensation was admitted to the hospital. He was moderately edematous and dyspneic; the pulse was rapid and collapsing. He was not thought to be in a grave condition and was given a tub bath, following which he became cyanotic and very dyspneic. Three minutes later there was frothing at the nose and mouth. Despite venesection, stimulation and artificial respiration he very shortly died. The blood Wassermann was subsequently reported as four plus. The clinical opinion was: (1) Syphilis; (2) aortic insufficiency (syphilitic); (3) acute myocardial insufficiency with pulmonary edema. This opinion seems to have been justified, as the autopsy revealed the evidences of syphilitic involvement of the aortic valve with aortic insufficiency. There was also a fibrous myocarditis with hypertrophy and dilatation. The point of special interest, however, was a rupture of one branch of the Y-shaped posterior papillary muscle close to the point of division. The chordæ tendineæ from the ruptured pillar led to the right half of the aortic leaflet of the mitral valve. The torn end of the pillar was rough and covered with adherent clot; in the central portion there was still recognizable a core of muscle encircled by a yellow opaque ring lying just beneath the endocardium. Microscopic sections revealed that the ruptured muscle was necrotic and a moderate number of spirochetes were demonstrated just beyond the necrotic area. The picture was not the classical picture of a gumma.

The authors review the very scanty literature on this subject without eliciting any further facts of interest. A somewhat similar case is reported by two Japanese observers, Nakajima and Ishiguro.⁷¹ The patient, a man, aged twenty-four years, died suddenly while performing strenuous muscular exertion. He had had syphilis for three years. At the postmortem a gumma was found in the auricular septum of the heart and another in the aortic orifice. This second gumma pressed on the left coronary artery and produced scar tissue in the posterior wall of the left ventricle near the apex and among the posterior papillary muscles. The immediate cause of death may have been a total occlusion of the left coronary.

CARDIAC ANEURYSM ASSOCIATED WITH HEART-BLOCK. What must be an extremely rare condition has recently been reported by Friedländer and Isaacs.⁷² The interest centers not only in an interventricular cardiac aneurysm of syphilitic nature, but in an associated heart-block

⁷⁰ Johns Hopkins Hospital Bulletin, 1921, xxxii, 30.

⁷¹ Bulletin of the Naval Medical Association of Japan, April, 1920, p. 1 (abstract, Journal of the American Medical Association.).

⁷² Journal of the American Medical Association, 1920, lxxv, 1778.

which seemed in all probability to have been due to the aneurysm itself. The heart was very large and showed syphilitic aortic endocarditis and mural endocarditis. In addition there was a dissecting aneurysm in the interventricular septum with an aneurysmal cavity measuring about 4.5 by 6. cm. This lay just below the median leaflet of the aortic valve which had a large perforation as its base. During life it had been recognized that the patient had syphilis, aortic insufficiency and heart-block, but no suspicion of the aneurysm had arisen, for in this case, as in the majority of instances of aneurysms of the heart, there was nothing to suggest the presence of such a lesion. A pericardial effusion had been diagnosed and was found, also widespread evidences of congestion.

The patient was too sick to be moved to the electrocardiograph, but polygraphic tracings confirmed the clinical diagnosis of partial heart-block. At one time a definite 3 to 1 rhythm was recorded. The Wassermann reaction was strongly positive and there is no reasonable doubt that the cardiac pathology had a syphilitic basis. It must be remembered that cardiac aneurysms are not always of syphilitic origin; they may result from any lessening of elasticity of the wall, as for example in the fibrosis of interstitial myocarditis, in fatty degeneration or where the wall is injured from new growths or disturbed circulation. The great majority, however, are due to syphilis and occur in males.

Notes on Cardiac Diagnosis. Modification of the second pulmonary sound is well known to occur in chronic diseases of the lungs and also in compensated mitral stenosis. Turrettini⁷³ states that changes in the character of the second pulmonary sound may be of great importance as the earliest sign of an oncoming pericarditis or endocarditis. He credits Jossierand, in 1907, with this observation. The characteristic change in tone is to a sharp ringing accentuation, and if this is observed in the course of an infection which is likely to involve the heart it is of great diagnostic significance. Once this altered sound is heard one must be on the watch for the friction of an early pericarditis or the murmur of a valvular involvement. It is much more frequently observed preceding a pericarditis, commencing at the base of the heart, than if the pericardial process has spread from the pleura to the pericardium.

An explanation for the frequent occurrence of accidental murmurs over the pulmonary artery has been advanced by Falkenhausen.⁷⁴ In his opinion such murmurs are the result of an abnormally close approximation of the pulmonary artery to the sternum. When the heart lies in the central or median position it lies closely against the anterior chest wall, and in this position it is probable that the pulmonary artery or the wedge of lung which may cover it is rubbed against the chest wall with each cardiac cycle.

DIAGNOSIS OF SO-CALLED "ACUTE DILATATION OF THE HEART." Levine⁷⁵ reports on 9 cases which might have been placed under this heading had not more careful study demonstrated the true nature of the attack. Levine, quite properly, points out that "acute dilatation

⁷³ Arch. d. mal. du cœur, etc., 1920, xiii, 440.

⁷⁴ Deutsch. med. Wchnschr., 1920, xvi, 1221.

⁷⁵ Journal of the American Medical Association, 1920, lxxv, 795.

of the heart" has long been a medical wastebasket for circulatory upsets occurring suddenly, both in patients known to have had heart disease and in those who previously have not suffered from cardiac disorders. Particularly has this term been loosely applied to sudden and alarming circulatory failure or collapse during or following surgical operations. Each of the 9 cases reported developed severe cardiac phenomena during or shortly after some surgical procedure. Seven of the patients had been under ether anesthesia, and procain, as a local anesthetic, had been used in the other two. Of the 9 patients it was found that 3 had paroxysms of auricular tachycardia, 4 suddenly went into auricular fibrillation and the other 2 had paroxysmal auricular flutter. All 3 of the cases of auricular tachycardia occurred while the patient was still unconscious; the other 6 patients had their upsets following operation at varying times, from twenty-four hours to nine days after operation. The attacks lasted from several minutes to several days in 7 cases, and in 2 the abnormal rhythm remained permanent as long as observations were made.

A proper differential diagnosis in such attacks is obviously of great importance, because on it will depend an intelligent and efficient management of the attack. As an illustration, one of the patients went into serious collapse while under ether anesthesia, and it seemed for some minutes that her life was in danger. The heart suddenly jumped to 216 and the breathing stopped. Artificial respiration was given, and, fortunately, the type of upset was paroxysmal auricular tachycardia, which generally can be arrested by vagal stimulation, either by direct pressure over the carotid arteries or by ocular pressure. In this instance, pressing rather vigorously on the left carotid artery caused a sudden cessation of the attack; the pulse dropped to 104 and the normal pink color replaced the former cyanosis. In the other two types of disorder this quick and dramatic result is impossible and cannot be hoped for. We are then dependent on proper digitalis therapy.

In the differential diagnosis the exact recognition of the abnormal mechanism may be difficult without special graphic methods, and confusion would be likely to arise between auricular flutter with a regular ventricular rate and auricular tachycardia. Auricular fibrillation should be recognized by the absolute arrhythmia without any semblance of a dominant rhythm. It might be helpful to remember that pressure on the vagus may slow temporarily the ventricular rate in an attack of flutter, but never stops an attack; on the other hand the rate of auricular tachycardia is rarely affected unless the attack is completely arrested. An abnormal regular rate in the vicinity of 200 per minute cannot be any other condition than auricular tachycardia, and in this condition the rate remains remarkably constant from minute to minute, not varying more than one or two beats per minute. In normal acceleration greater variations are found. It is urged that well-defined terms which actually describe the abnormal mechanism be employed when possible rather than the vague name "acute dilatation of the heart."

AURICULAR HEART SOUNDS are described by Reid.⁷⁶ This author is

⁷⁶ *Journal of the American Medical Association*, 1921, lxxvi, 928.

not satisfied with the troubles we have incident to three heart sounds, but suggests that there are actually five heart sounds with each cardiac cycle. These five are the first and second auricular, the first and second ventricular and at times the so-called third heart sound. We may be forgiven for not hearing the sounds produced by auricular systole, as they are faint and may often be below the level of audibility. It is only in cases of heart-block, when the auricular contractions may occur well separated from those of the ventricles, that the auricular sounds can be detected. The interval between the two auricular sounds is claimed to be almost *nil* and the vibrations of the second sound may well fill the interval known as the auriculo-ventricular intersystolic period, and so be merged in the first ventricular sound. This intersystolic period, the occurrence of which Lewis denies, is measured by others as occupying 0.055 second.

INSTANTANEOUS ROENTGENOGRAMS OF THE HEART at determined points in the cardiac cycle have been made by Eyster and Meek.⁷⁷ The recording of simultaneous electrocardiograms permits the exact point in the cardiac cycle at which the roentgenograms were taken to be determined. Two exposures can be made during one cardiac cycle. By this method the changes in the size and shape of the human heart during its cycle can be studied. The most important points which have been determined are: (1) The movement of no single border of the heart is an accurate index of the extent of its contraction; the whole outline is necessary for such estimation. (2) The mechanism of ventricular filling would seem to be very similar to that which physiological experimentation has constituted in the dog, especially in that the major part of ventricular filling occurs shortly after the ventricle goes into relaxation and is in large part completed before the subsequent auricular contraction, systole of this chamber playing little rôle in adding blood to the ventricles.

Arrhythmia and Electrocardiography. By far the most important work in this field has been that of Thomas Lewis⁷⁸ and his associates, Feil and Stroud. The international nature of scientific research is well exemplified by these reports, some of which are the result of the investigations carried on by this eminent British cardiologist with the assistance of two American workers. The four extensive articles which form this series are entitled "Observations upon Flutter and Fibrillation." In Part I the extreme regularity of clinical auricular flutter is emphasized and the limits of variation in the lengths of the intra-auricular cycles are determined. Lewis states that it seems advisable that the term auricular flutter should be confined to disorders, be they clinical or experimental, in which comparable variations in the lengths of auricular cycles are found not to be exceeded.

In Part II experimental evidence is advanced to show that auricular flutter, as produced in the dog, is identical with auricular flutter as this is observed in the human subject. Just as in human flutter the rate of the auricular movements is very rapid, the movement of the auricle

⁷⁷ American Journal of Roentgenology, 1920, vii, 47.

⁷⁸ I, Heart, 1920, vii, 127. II, Ibid., p. 191. III, Ibid., p. 247. IV, Ibid., p. 293.

shows a high grade of regularity and the auricular complexes are contiguous and uniform in outline. By studying this auricular flutter in the dog, Lewis and his associates have been able to demonstrate that the excitation wave passes through the auricular tissue in a perfectly regular sequence from cycle to cycle over considerable periods. In a number of instances it was found that the wave took a definitely circular course around the orifice of the superior vena cava and near or around the mouth of the inferior vena cava. The movement of the excitation wave may be in either direction in this ring and it forms what is referred to throughout as a "continuous circus movement." As a result of this circular movement there is no true diastole of the whole auricle at any one time, for at every instant some part of the auricular tissue is becoming activated. From this central circular "circus movement" excitation waves are thrown off centrifugally to other portions of the auricles, as, for example, the appendages. Such a constant "circus movement" of the excitation wave would constitute a mechanism which would explain long-continued flutter in the human subject and the high rate of auricular beating.

Part III is concerned with further studies of the after-effects of stimulation of the mammalian auricle by means of rhythmic induction shocks. Pure flutter, impure flutter or fibrillation may develop. Flutter may end abruptly and the manner of its termination is compatible with the theory that flutter is constituted by a circus movement in the auricle.

In Part IV impure flutter is explained. It differs from pure flutter only in that the excitation wave spreads with less uniformity over the auricle from cycle to cycle. Apparently local obstructions or actual barriers (block) may interfere with the movement of the excitation wave and deflect it along new and sinuous paths. When this process involves not only the outlying regions of muscle, but also the path of the central wave, it is imagined that auricular fibrillation, as it is spoken of clinically, sets in. These observations serve to link up pure flutter, impure flutter and auricular fibrillation, and they help to explain the close interrelation of all these conditions. Flutter, for example, may be brought to an end in the human subject by means of digitalis; it is converted into fibrillation, which subsequently often gives place to the normal rhythm as the effect of the drug wears off. It is tempting, Lewis says, to conclude that the change from flutter to fibrillation is brought about by digitalis as a result of a still unproved depressive action of this drug on conduction in the auricular muscle. In other words, digitalis may change flutter to fibrillation by so interfering with auricular conduction as to break the circus movement of the excitation wave which was keeping up the flutter. As Lewis suggests, if this is the method of action of digitalis in such cases then much simpler and more efficient remedies at once suggest themselves. These are at present being investigated.

A clinical case which bears on these views concerning the change of auricular flutter to fibrillation is reported by Bishop.⁷⁹ The patient suffered an attack of frightful rapidity of the heart which lasted over a

⁷⁹ Journal of the American Medical Association, 1921, lxxvi, 787.

period of several days. In two leads of the electrocardiograms all the characteristics of fibrillation of the auricles were shown. In the other lead, however, were found a number of beats with normal rhythm except for one auricular premature contraction. The patient was taking digitalis in considerable doses. From the history and the presence in the electrocardiograms of the normal beats it was suspected that the case was one of fibrillation due to digitalis effect in an attack of flutter. The digitalis was therefore entirely stopped and the heart resumed a normal rhythm. Bishop concludes that it is good policy to keep a certain amount of digitalis in the system of people who suffer from repeated attacks of auricular flutter, so that an attack may be more quickly controlled when it occurs.

The differential diagnosis of various forms of rapid heart by the use of simple bedside means is well discussed by Levine.⁸⁰ This report offers practical assistance both in diagnosing such attacks and in the treatment of them. It deserves to be read in the original. That harm may be done by misdirected treatment in this group of cases is suggested not only by Bishop's report, but also by a report from Rome by Galli.⁸¹ He found that in a case of undoubted paroxysmal tachycardia the administration of atropine tends to provoke the tachycardial attacks. The result was the same whether the atropine was injected hypodermically or given by the mouth, except that the interval before the attack came later (about one hour after taking the atropine) if the oral method of administration was resorted to. One milligram of atropine was sufficient to provoke a typical paroxysm, and when massive doses were given the tachycardial effects were more evident and constant.

HEART-BLOCK. What is probably the most marked case of bradycardia on record is reported by Odrizola.⁸² The original article is not available, but the abstract states that on one day the pulse-rate was eight per minute and the next day there were intervals of fifty and fifty-eight seconds between the beats. Necropsy, the third day, revealed two gummas of the auriculo-ventricular septum; the bundle of His had been destroyed by the syphilitic disease. In heart-block it is not unusual that a venous pulse is seen in the veins of the neck. Visible venous pulse in the femoral vein is a very rare phenomenon. Its occurrence in a case of complete heart-block is reported by Pezzi, Donzelot and Yacoel.⁸³

Calvin Smith⁸⁴ reports a case of high-grade heart-block in a young man, aged twenty years, with no symptoms whatever. His first attack of unconsciousness occurred at the age of three years and attacks continued to occur at intervals of perhaps three or four months until the age of nine years. No syncopal attacks since that time. No etiology was found and the Wassermann was negative. Apparently complete heart-block was present all the time, but following forcible expiration

⁸⁰ Boston Medical and Surgical Journal, 1921, clxxiv, 53.

⁸¹ Heart, 1920, vii, 111.

⁸² Anales. d. l. fac. d. med. d. Lima, 1920, iii, 5 (abstract, Journal of the American Medical Association).

⁸³ Arch. des mal. du cœur, etc., 1920, xiii, 97.

⁸⁴ Journal of the American Medical Association, 1921, lxxvi, 17.

there ensued a normal sequence of auriculo-ventricular activity. The author advances no explanation for this unusual combination of findings.

AURICULAR FIBRILLATION. The mortality in auricular fibrillation, as determined by Willius⁸⁵ from an analysis of 500 cases, was found to be much greater than that occurring in similar types of heart disease not complicated by this variety of arrhythmia.

"Perpetual arrhythmia" is a term which was formerly often applied to auricular fibrillation, but, as Lutembacher⁸⁶ points out, several types of arrhythmia, each with a different cause and requiring a different treatment, were included under the one term. In this group is included extrasystoles, auricular flutter, etc.

NOTES OF ELECTROCARDIOGRAPHIC INTEREST. Last year mention was made of the reports concerning "bundle branch block," or, in other words, a block of one of the branch of the bundle of His. Wilson and Herrmann⁸⁷ confirm the fact that complete bundle branch block produces characteristic changes in the form of the ventricular complex both in animals and in man. They do not, however, agree entirely with those who have attempted, from changes in the form of the ventricular complex, to diagnosticate so-called "arborization block," which is claimed to be produced by lesions of the subdivisions of the branches of the His bundle or their arborizations. An electrocardiographic sign of coronary artery obstruction has been described by Pardee.⁸⁸ It was first observed in a patient who had just had an attack typical of occlusion of a coronary artery, and five other similar records have been found; four of these five gave a history of typical attacks of anginal pain while the other had slight precordial pain on exertion. Experimental work on dogs agrees with these findings. The characteristic changes appear a day or two after obstruction. The *Q R S* group is usually notched in at least two leads and usually shows left ventricular predominance. In Lead I or III the *T*-wave does not start from the zero level of the record and quickly turns away from its starting-point in a short curve. The *T*-wave is usually of a larger size than customary and is usually turned downward in Lead II and in one other lead. Pardee's patient recovered from the acute attack, lived for two years and died with a typical attack of angina pectoris. The electrocardiogram retained its changed form from the fourth day after the attack for four months.

The value of the electrocardiograph in prognosis is emphasized by Heard and Hein.⁸⁹ They point out that as cardiac failure is due to myocardial insufficiency the electrocardiograph can furnish valuable information from the standpoint of prognosis. They also point out that although it is the internist who has the greatest skill in interpreting clinical evidence as to the imminence or presence of cardiac failure, yet it is the internist who most frequently avails himself of the help of the electrocardiograph.

⁸⁵ Minnesota Medicine, 1920, iii, 365.

⁸⁷ Archives of Internal Medicine, 1920, xxvi, 153.

⁸⁸ Ibid., p. 244.

⁸⁹ American Journal of the Medical Sciences, 1920, clx, 828.

⁸⁶ Paris méd., 1920, x, 85.

Anomalies of the *P*-wave were found by Hamburger⁹⁰ to be associated, in the majority of cases, with varying degrees of myocardial insufficiency. Inversion of the *P*-wave with auricular extrasystoles should probably be interpreted as evidence of auricular pathology; without extrasystoles, it is probably due to variations in vagus control.

PAROXYSMAL TACHYCARDIA. A most interesting case is reported by Fussell and Wolferth⁹¹ in which in the intervals between typical attacks of paroxysmal tachycardia there occurred periods of slow auriculo-ventricular rhythm with a constant shifting of the pacemaker back and forth between the sinus and the auriculo-ventricular nodes. During the periods of auriculo-ventricular rhythm the rate was about fifty per minute; the attacks of paroxysmal tachycardia were typical, with a rate about 135 per minute. The patient had had the attacks for forty years, being sixty-two years of age at the time of this report, and she had for many years been able to control the majority of the attacks by holding her breath for a considerable length of time, perhaps fifteen seconds. This is unusual, and the more usual methods by vagus or ocular pressure were in this case unsuccessful. Following the termination of the tachycardia a pause would be followed by an isolated contraction and another pause. Sometimes these pauses would be as long as four or five seconds. The first beats would be of supraventricular origin, but later the fairly slow auriculo-ventricular rhythm would become established, interrupted by short runs of sinus rhythm. This behavior of the heart, following the interruption of the tachycardia, is unique. All the evidences of severe myocardial disease were present and the patient died soon after these observations were made.

Feil and Gilder⁹² have found that the curves in paroxysmal tachycardia show a high degree of regularity, approaching that already referred to in clinical auricular flutter.

Paroxysmal tachycardia of ventricular origin is of more serious prognostic import than that of auricular origin and the differentiation of the two types is of practical importance, according to Robinson and Herrmann.⁹³ In some of the cases there exists a relationship between this tachycardia and occlusion of the coronary vessels.

BRADYCARDIA. Willius⁹⁴ has discussed chronic bradycardia on the basis of a study of 227 patients. The cases were subdivided into groups: (1) Those with myocardial disease; (a) with lesions of the auriculo-ventricular bundle, and (b) without involvement of the bundle; (2) endocardial valvular disease, and (3) vagus augmentation. Each of these groups is analyzed separately in subgroups according to the degree of bradycardia. He gives the following summary of the causes generally accepted as causing "slow heart."

1. *Chemical Substances.* The inhibitory action of the following substances is well known and warrants no discussion here: (a) The neutral non-nitrogenous glucosides and resins; the active principles of digitalis, squill, strophanthus and apocynum; (b) alkaloids such as erythrophlein,

⁹⁰ Archives of Internal Medicine, 1920, xxvi, 232.

⁹² Heart, 1921, viii, 1.

⁹⁴ Archives of Internal Medicine, 1920, xxvi, 630.

⁹¹ Ibid., p. 192.

⁹³ Ibid., p. 59.

veratrine and aconitine; (c) biliary constituents, and (d) inorganic substances, such as barium salts and hydrates.

2. *Stimulation of the Cardiac Vagus.* Stimulation may be peripheral or central.

3. *Myocardial Disease.* Involvement of the myocardium by disease (a) associated with lesions of the auriculo-ventricular bundle (complete heart-block and delayed impulse transmission), and (b) without involvement of the bundle.

4. Certain physiological reactions without cardiac damage.

5. The early and late stages of asphyxia.

Gallavardin and Gravier⁹⁵ report on "Permanent Nodal Bradycardia." This type of bradycardia, which is also called auriculo-ventricular rhythm, should be considered the equivalent of a total sino-auricular block, and depends, in all probability, on destructive lesions of the sinus node or of its lower fibers of connection.

Treatment in Heart Disease. The importance of prevention of heart disease is obvious and mention has been made both last year and in this present article of some figures which suggest that possibly something is being accomplished along this line. The problem is an enormous one, as is well emphasized by Conner.⁹⁶ He states that among 5,000,000 men of military age more than 200,000 were disqualified for service because of heart defects, while in 1917, in the United States registration area, diseases of the heart were responsible for almost one-eighth of the deaths of all ages, and for almost one-fifth of the deaths in persons of forty years of age or over. He urges an appreciation of the problem and active organization to meet it by several measures; the encouragement of the formation of special cardiac dispensary classes; the increasing of facilities for the care of suitable heart patients in convalescent homes; the arousing of greater interest in the welfare of school children with heart disorders, and a concerted attack at the problem, both of prevention and treatment, by investigators, clinicians and public health organizations. Special organizations and heart clinics should be encouraged. Poynton⁹⁷ also points out that the study of heart disease should commence in the young and that it is by prevention that the most can be accomplished. Had the same energy been expended on acute rheumatism as has been on tuberculosis and venereal affections the study of heart disease would have already made substantial progress.

DIGITALIS IN HEART DISEASE. Luten⁹⁸ thus summarizes the effect of digitalis on the heart.

"It may be said that digitalis stimulates the vagus when administered clinically: that this stimulation affects chiefly conductivity and that by blocking off from the ventricle many impulses to contraction in cases of decompensation showing auricular fibrillation (or flutter), it protects the ventricle and allows it to rest and restore its efficiency. It may be said, further, that while it has been shown that digitalis

⁹⁵ Arch. des. mal. du cœur, etc., 1921, xiv, 71.

⁹⁶ Journal of the American Medical Association, 1920, lxxiv, 1564.

⁹⁷ British Medical Journal, 1920, ii, 882.

⁹⁸ Journal of the American Medical Association, 1921, lxxvi, 26.

has an effect on the heart muscle, the exact nature of this effect is not known, and that there is at present a difference of opinion as to whether there is any benefit to be derived from administering the drug to patients showing a normal mechanism. In most such cases, indeed, there appears to be no contraindication to its use; but its well-known effect in causing premature contractions should be kept in mind. While these, of course, are usually disregarded, it is nevertheless possible that in a case showing a marked tendency toward premature ventricular contractions the effect of large doses of digitalis might be just enough to produce ventricular fibrillation, which, indeed, is described by pharmacologists as the end-result of an overdose."

Last year considerable space was devoted to a discussion of the so-called Eggleston method of administering digitalis in large single doses, and the advantages of this method were enumerated. Since then Eggleston⁹⁹ has reviewed the subject and given the newer concepts in digitalis therapy. His review is excellent but adds little to what was noted last year. Robinson¹⁰⁰ advocates single large doses of from 15 to 25 cc of the tincture in certain cases of heart disease, provided the tincture is standardized, the dosage regulated and the patient is kept under close observation.

Pardee¹⁰¹ has made a clinical study of the rate of absorption of digitalis from the gastro-intestinal tract, and, as a result, comes to the following conclusions: That when given by the mouth, digitalis is absorbed rapidly enough to affect both heart-rate and heart muscle in from two to four hours; that the effect reaches its maximum at six or seven hours and is maintained at least approximately for twenty-four hours. He recommends that when a tincture of unknown potency is to be employed as a single large dose the limit of one minim of the tincture per pound of body weight should never be exceeded. The administration of such a dose is inadvisable except in the presence of urgent heart failure, when the patient is in bed and when prompt results are demanded. It should never be attempted under any circumstances if the patient has received any preparation of digitalis or its allies within a period of two weeks. A twenty-four-hour interval between doses would appear to be quite satisfactory for maintaining a continuous effect and a daily dose of 20 minims will suffice in the great majority of patients to maintain the desired digitalis effect which has been produced by a series of larger doses. It is inadvisable to give a second dose within six hours after an initial large dose has been administered, for the full effect of the first dose will not be manifest until this time has elapsed.

Effect of Therapeutic Doses of Digitalis. Experimental evidence has been presented by Cohn and Levy¹⁰² that therapeutic doses of digitalis and strophanthin, equal to about 30 per cent of the calculated lethal dose, do increase the contractile power of the cardiac musculature, and by so doing increase the volume output. It is well known that digitalis

⁹⁹ American Journal of the Medical Sciences, 1920, clx, 625.

¹⁰⁰ Southern Medical Journal, 1920, xiii, 396

¹⁰¹ Journal of the American Medical Association, 1920, lxxv, 1258.

¹⁰² Proceedings of the Society of Experimental Biology and Medicine, 1920, xvii, 160.

does benefit in many conditions in which there has been no experimental proof of its value; in fact, in therapeutic doses the only condition in which evidence has been previously presented that digitalis is beneficial is in cases of fibrillation of the auricles. In auricular fibrillation it is by producing a block of the auricular impulses that digitalis accomplishes at least part of the benefit. In the experiments conducted by Cohn and Levy on dogs and cats, not only were the contractile power of the heart muscle and the volume output increased, but there occurred a transient elevation of blood-pressure. In more than half of the animals there occurred a change in the *T*-wave of the electrocardiogram.

Mackenzie¹⁰³ in an article on the idioventricular rhythm discusses the application of his theory of "disturbed reflexes" to the action of digitalis. It is his belief "that the mechanism by which many symptoms are produced is due to the modification of reflexes that are normally present in the body." According to this theory, in the vast majority of people who have a rapid action of the heart there is present some disease which produces agents that act upon the cardiac reflexes. In such cases digitalis fails to act because the reflex is already poisoned by an agent which the digitalis is unable to overcome; such a condition is found in pneumonia, influenza and measles. In auricular fibrillation and in the idioventricular rhythm described by Mackenzie the rapid pulse-rate is due to a totally different cause, and digitalis is active in these cases for the reason that the reflex on which it acts has not been disturbed by any other toxic agent.

Studies of the Drug Digitalis. Clinicians have long held the opinion that the action of the tincture of digitalis differs qualitatively as well as quantitatively from that of the infusion. Weiss and Hatcher¹⁰⁴ have been unable to discover any experimental evidence to support this view. It is true that the official infusion does not represent the drug completely, hence the standardization of the leaf does not ensure uniformity in activity of the infusion. This variability is at the expense of the more absorbable of the active principles. The authors, however, present a simple method of preparing the infusion by which the above variability is avoided and the activities of the leaf are completely represented. An infusion thus prepared has these advantages over one made according to the present Pharmacopœial method:

1. There is better extraction, whereby the infusion represents the activities of the drug completely.
2. There is uniformity of activity in place of the variability of the official.
3. With a given degree of activity it contains a larger proportion of the slightly soluble, but more readily absorbable, digitoxin or digitoxin-like substance or substances.
4. The dosage is just ten times that of the tincture in volume.
5. The filtered infusion is transparent.
6. It may be kept indefinitely without loss of activity. In fact, it has been kept in completely filled and hermetically sealed bottles for more than two years and five months with its activity unimpaired.

¹⁰³ Lancet, 1921, i, 681.

¹⁰⁴ Journal of the American Medical Association, 1921, lxxvi, 508.

On the other hand, Pomeroy and Weyl¹⁰⁵ came to the conclusion that the infusion is slightly less active than the tincture. They also concluded that, owing to deterioration, infusions should be discarded in from three to seven days time, depending on the temperature. The addition of alcohol did not add to the stability of the infusion.

Hatcher¹⁰⁶ has described a chloroform-soluble digitalis body which exerts the typical cardiac action of digitalis. It resembles digitoxin somewhat and is not more actively emetic than is digitalis in proportion to its therapeutic effects. Hatcher believes that it is suitable for administration in any of the usual ways. His report states that further pharmacological studies were in progress. Eggleston¹⁰⁷ compared the absorption of this chloroform-soluble extract from the human alimentary canal with that of various tinctures of digitalis. It was found to be absorbed at least as rapidly as the best tincture of digitalis, and its persistence of action is apparently of the same order as that of digitalis of the best grade. It is interesting to note that wide differences were found in the rapidity and completeness of absorption of tinctures derived from a variety of sources. Some of these showed very poor absorption, but the absorption of the chloroform-soluble extract was markedly uniform and satisfactory. It is to be hoped that these reports will lead to the perfection of a uniform standardized preparation of digitalis, of which we are much in need. There is a vast difference in the preparations on the market, and if a standardized preparation were available we could better resist the high-priced special preparations which are so glowingly offered. As West and Pratt¹⁰⁸ say: "Few clinicians have available the material or skill for assaying the drug they must use in so many important cases. The *Pharmacopœia* has set a standard for the minimum activity of acceptable leaf, yet this does not solve the problem entirely, since wide variations in potency are found above this minimum required. In spite of this requirement, much of the digitalis on the market today is below standard, while occasional samples are found considerably above the Pharmacopœial strength. It is further difficult to judge without making actual assays how much the original leaf or the preparation may have deteriorated in strength before the drug comes into the hands of the physician." In an effort to meet this problem, experiments were carried out with a standardized dried aqueous extract of digitalis, with hopeful results.

TREATMENT WITH OTHER DRUGS THAN DIGITALIS is often neglected because of the greater value and efficiency of digitalis. There are indications, however, which must sometimes be met without the administration of digitalis or even of the closely related drug strophanthus. Concerning strophanthus, little has been written recently; a few general articles advocate the intravenous administration of strophanthin despite the danger which is associated in certain cases with this treatment.

¹⁰⁵ American Journal of Pharmacy, 1920, xcii, 394.

¹⁰⁶ Journal of the American Medical Association, 1920, lxxv, 460.

¹⁰⁷ Ibid., p. 463.

¹⁰⁸ Journal of the American Medical Association, 1920, lxxv, 77.

Mory¹⁰⁹ even advises its use coincidently with digitalis medication by the mouth.

Squill has long been considered to be a digitalis-like drug, and studies by White, Balboni and Viko¹¹⁰ confirm this view. These investigators found that squill does have a definite digitalis-like action, but only in larger dose than that now stated as an average, *e. g.*, from 2 to 4 drams (8 to 16 cc) instead of 15 minims (1 cc) of the tincture at each dose. It was suggested, in the discussion of this article, that this relative inactivity of squill is probably due to the fact that squill is poorly absorbed from the gastro-intestinal tract.

Choral is advised by Glaus¹¹¹ for the treatment of insomnia in cardiovascular disease, especially in cases with high blood-pressure. It may be given over long periods without apparent harmful effects. He even claims an increased diuresis following its use. The usual dose is between 15 and 30 grains (1 and 2 gm.).

Quinine and quinine derivatives are employed in the treatment of paroxysmal tachycardia and even of auricular fibrillation. Most of this work is still in the experimental stage and final opinion will have to be postponed. Schrumpf¹¹² advises it in conjunction with digitalis, and states that before fibrillation commences this treatment is especially helpful in preventing or delaying the onset of the fibrillation.

In 1914 Wenckebach recorded 2 cases in which auricular fibrillation was converted to normal rhythm after the administration of quinine. In 1918 Frey found that quinidine was the most active cinchona derivative therapeutically. Recently, Levy¹¹³ has studied the effectiveness of this preparation in the restoration of the normal cardiac mechanism in auricular fibrillation. He states that the foreign literature of the past three years contains reports of 101 cases of auricular fibrillation treated with quinidine; in 59 the normal rhythm was restored for periods up to four months. Levy has studied the action of the drug in patients and experimentally, but is unable as yet to explain the method by which the drug acts. The drug is toxic and must be used with care. At present the information is not sufficient to advise the employment of the drug in cases not under the most careful observation. Further data will undoubtedly soon be published. Jenny¹¹⁴ gives 0.5 gram of quinidine two or three times a day, and states that 2 or 3 grams a day can be given without danger. Seventeen of his 18 cases had a normal rhythm restored by the drug. Clerc and Pezzi¹¹⁵ consider quinine as a drug which lessens overexcitability of the cardiac muscle.

Adrenalin has been employed, as, for example, during an operation. The work of Levine, referred to elsewhere in this review, emphasizes the importance of proper diagnostic interpretation of such attacks and the necessity of having the treatment directed according to the nature of the attack. Vogeler¹¹⁶ injected 15 minims (1 cc) of a 1 to 1000

¹⁰⁹ München. med. Wehnschr., 1920, lxvii, 570.

¹¹⁰ Journal of the American Medical Association, 1920, lxxv, 971.

¹¹¹ Schweiz. med. Wehnschr., 1920, l, 841.

¹¹² Presse méd., 1920, xxviii, 524.

¹¹³ Journal of the American Medical Association, 1921, lxxvi, 1289.

¹¹⁴ Schweiz. med. Wehnschr., 1921, li, 272.

¹¹⁵ Médecine, 1921, ii, 443.

¹¹⁶ Deutsch. med. Wehnschr., 1920, xlv, 740.

solution of adrenalin directly into the heart of a patient who had collapsed, within a minute he improved, but despite further measures this proved merely temporary and the patient died. That the effect of adrenalin on the heart may not always be beneficial is pointed out by Lutembacher¹¹⁷ in connection with cases of total and partial heart-block. In such cases the effects may be very serious at once, or, if the primary results are recovered from the heart may be dangerously slowed for several days. Henschen¹¹⁸ has also employed intracardiac injections in the attempt to resuscitate the heart, and claims success. He details the points to be preferred for the injection. In such efforts at resuscitation it is interesting to note that Fisher¹¹⁹ states that it is useless to attempt to revive the heart if there has been a cessation of circulation for thirty minutes. After this period cardiac massage, artificial respiration or other measures are without avail. Gunn¹²⁰ advises the injection of adrenalin into an external jugular vein in such cases, this to be followed by massage of the heart and artificial respiration.

Non-medicinal Treatment. Much is being accomplished in the after-care of cardiac cases, especially in children, by special cardiac clinics and by a greater appreciation of the importance of the regulation of the individuals with crippled hearts in every phase of their life and activity. The description of such a clinic, given by Bopp,¹²¹ is most interesting. In a recent article by Pellini,¹²² one will find some helpful suggestions for the management of such a cardiac clinic in a practical way.

In acute endocarditis in children the importance of rest cannot be overemphasized. Ledford¹²³ does not allow the severely ill children even to feed themselves. The disease was treated as an acute infectious disease and digitalis was used very infrequently—in fact, only in cases of chronic valvular lesions with failure of compensation.

Intravenous transfusions of blood from a donor immunized by vaccine injections were used by Levison¹²⁴ in a case of infectious endocarditis due to the streptococcus. Four transfusions were given, each of about 500 cc. The beneficial results of the added blood were obvious, but apparently there was no curative effect; the temperature curve was not influenced nor the pulse-rate reduced. A fatal outcome was apparently not much delayed.

Diseases of the Aorta. ANEURYSM. There is little new in the recent literature on this subject, but several articles properly emphasize some of the less generally appreciated points.

Aneurysm of the thoracic aorta is rare in children, but does occur occasionally. Calvin¹²⁵ has collected 35 cases from the literature, and he reports 2 of his own cases in which the process was due to an acute infectious aortitis. In both his cases there was a clear history of infec-

¹¹⁷ Presse méd., 1921, xxix, 145.

¹¹⁸ Schweiz. med. Wchnschr., 1920, I, 261.

¹¹⁹ British Medical Journal, 1920, ii, 698.

¹²⁰ Ibid., 1921, i, 9.

¹²¹ Journal of the American Medical Association, 1920, lxxv, 1587.

¹²² Ibid., 1921, lxxvi, 774.

¹²³ American Journal of Diseases of Children, 1921, xxi, 139.

¹²⁴ Journal of Laboratory and Clinical Medicine, 1921, vi, 191.

¹²⁵ American Journal of Diseases of Children, 1921, xxi, 328.

tion. Such cases of infectious aortitis resulting in aneurysm are of great interest and importance, but must be kept clearly separated from aneurysms due to some congenital defect or of syphilitic nature. To what extent congenital syphilis may affect the aorta, and whether it may ever bring about juvenile aneurysm, is still under discussion.

In a clinic on aneurysm of the thoracic aorta, Landis¹²⁶ reports a case of a boy, aged thirteen years. The patient was a colored boy who complained of slight cough and expectoration. He had noticed for the past six months that he was short of breath after exertion. He was somewhat under his best weight. On examination there could be seen an area of pronounced pulsation in the second and third interspaces and extending about one inch to the right of the sternum. The pulsation could be felt, but there was no thrill nor diastolic shock. The area gave a dull note on percussion. On auscultation there was heard a double aortic murmur, the diastolic portion of which was best heard in the third left interspace near the sternum. The heart was slightly enlarged both to the right and to the left. Roentgenological examination revealed a widened arch with a pronounced expansile pulsation, especially marked in the first portion of the aorta. Landis states that he had little doubt as to the correctness of the diagnosis of aneurysm, but that the cause was difficult to determine. There was no obvious infection and two Wassermann tests had been negative. The other cases reported by Landis are more classical and well illustrate; as he says, how readily aneurysm of the thoracic arch may be overlooked. One must rid one's mind of the conception that the recognition of a thoracic aneurysm depends on the presence of a tumor mass which has the characteristic heaving, expansile pulsation, or that in the absence of bulging there is a definite area of pulsation. If one depends on such criteria the great majority of thoracic aneurysms will go unrecognized.

Although in children one thinks first of some congenital defect or of acute infection as the cause of an aneurysm, in adults syphilis is one's first thought. Martinet¹²⁷ found a history suggesting syphilis in 24 of his 29 patients with aneurysm of the aorta. Whether tuberculosis ever causes aneurysm of the aorta is in doubt. By analogy with the so-called Rasmussen's aneurysm of the pulmonary artery which is due to tuberculosis, one might expect a similar involvement of the aorta. Letulle¹²⁸ has reported five cases of Rasmussen's aneurysm.

Rupture of Thoracic Aneurysm. It is generally believed that in about one-half of all cases of aneurysm of the thoracic aorta death occurs from rupture of the aneurysm. A discussion of this point is given by du Bray¹²⁹ in connection with the report of a saccular aneurysm of the descending thoracic aorta which ruptured directly into the lower lobe of the left lung and the left pleural cavity. In the figures quoted by du Bray the left pleura and left lung appear to be frequent seats for the

¹²⁶ Medical Clinics of North America, 1921, iv, 1083.

¹²⁷ Presse méd., 1920, xxviii, 733.

¹²⁸ Bull. et mém. d. l. Soc. anatom., Paris, 1920, xvii, 6.

¹²⁹ American Journal of the Medical Sciences, 1921, clxi, 407.

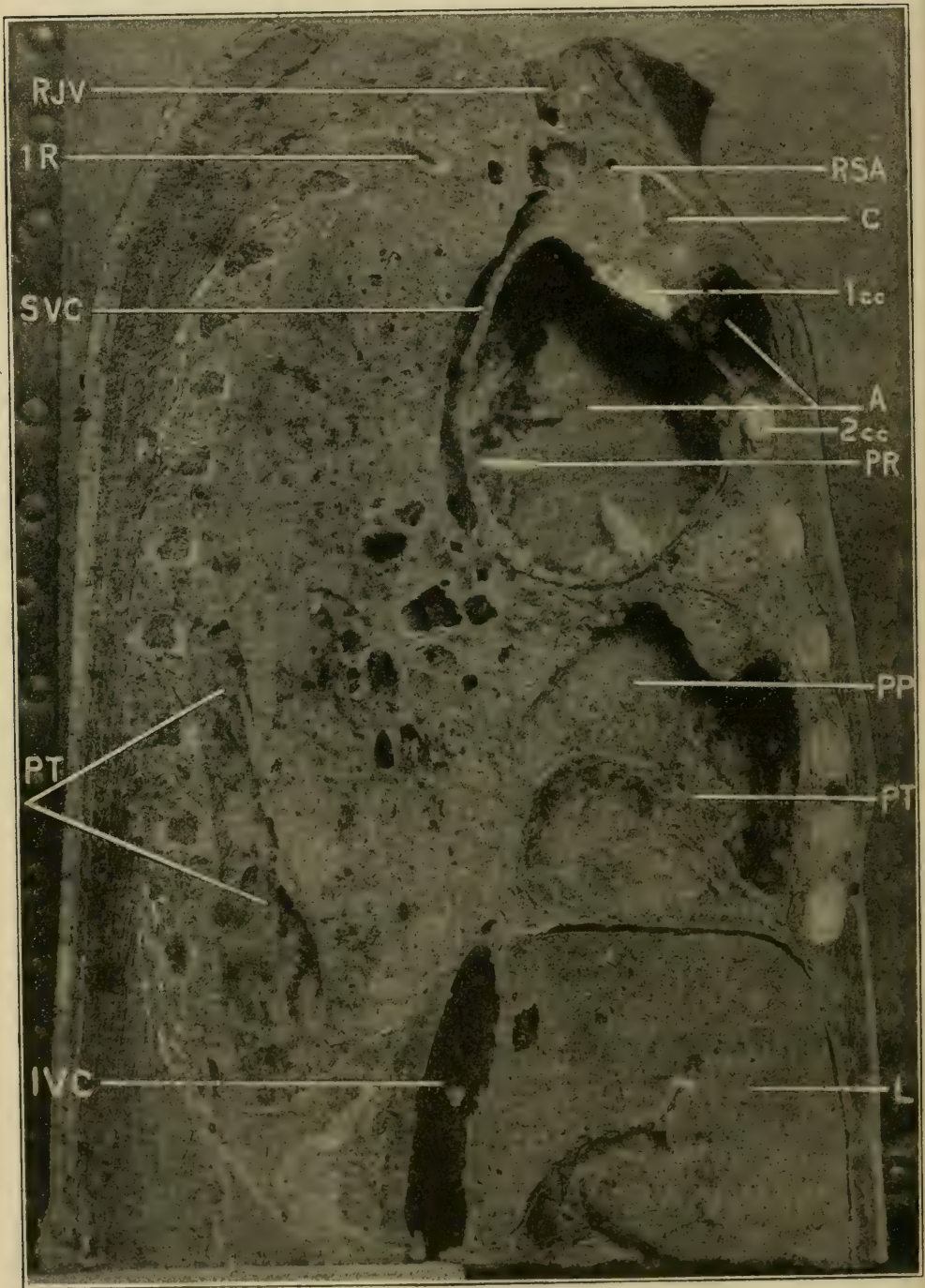


FIG. 1.—*RIV*, right internal jugular vein; *IR*, first rib; *SVC*, superior vena cava; *PT, PT*, pleural transudate; *IVC*, inferior vena cava; *L*, liver; *P-P*, pleuro-pericardium; *PR*, probe in opening between trachea and aneurysm; *2CC, 1CC*, second and first costal cartilages; *A*, aneurysm; *C*, clavicle; *RSA*, right subclavian artery.

rupture. He also discusses hemoptysis in aortic aneurysm, and concludes that it must be regarded as a symptom of thoracic aneurysm, and it may be frequent and persistent before a fatal hemorrhage occurs.

Norris and Fetterolf¹³⁰ have recently published some excellent photographs of frozen sections from a case of protruding aneurysm of the arch of the aorta. The patient was a negro laborer, aged thirty-nine years; the Wassermann test was positive; diagnosis was evident on physical examination and the roentgen-ray study was confirmatory. The patient appeared to die from pressure and from exhaustion. Although no blood was coughed up the trachea was filled with it. It seems not unlikely that rupture may account for more deaths than purely clinical records without a postmortem would lead us to believe.

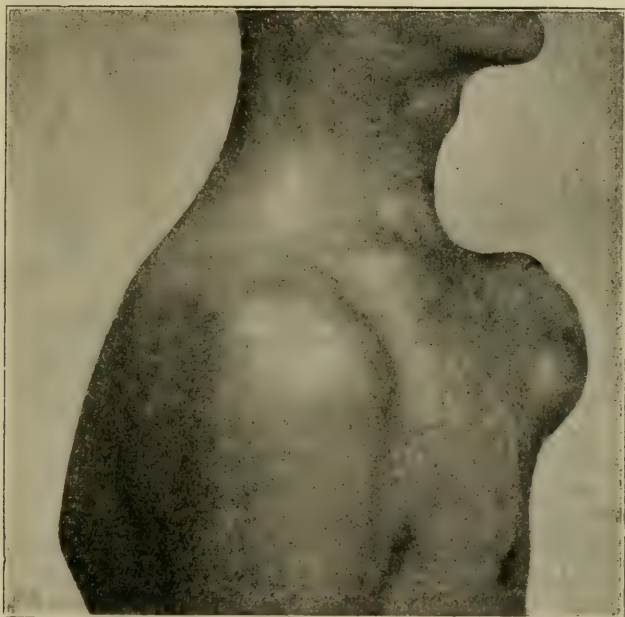


FIG. 2.—Case II. Right lateral view of aneurysm.

In the illustration here reproduced one can see a probe passing through the perforation of the aneurysm into the trachea. The sternum is intact, the aneurysm having protruded between the ribs.

Wiring of Aortic Aneurysms. Hare¹³¹ has reported 3 additional cases of aortic aneurysm treated by wiring and electrolysis with remarkably excellent results. In each of these 3 cases there was marked relief of pain and in at least 2 of the cases considerable lengthening of life. One case was wired on December 1, 1919, and was reported doing finely on September 27, 1920; another was wired May 26, 1920, and was in good condition and doing his daily work on December 6, 1920. The other case was much more advanced, as can be seen by the photograph

¹³⁰ Archives of Internal Medicine, 1920, xxvi, 114.

¹³¹ Journal of the American Medical Association, 1921, lxxvi, 587.

here reproduced (Fig. 2). In this most unfavorable case there was relief of the boring pain after the wiring and the patient lived in comparative comfort for two months and nine days. Death occurred from rupture into the esophagus.

Miscellaneous Notes on the Aorta and Aneurysms. Moon¹³² reports a case of congenital stenosis of the aorta in a boy, aged eleven years. He had never had any marked symptoms, but had always become breathless sooner than other boys.

Congenital aneurysm of the aortic sinus of Valsalva is to be regarded as an anatomical curiosity according to Goehring.¹³³ Clinically, because of their bizarre manifestations, their diagnosis during life has been difficult or impossible.

Manouélian¹³⁴ reports finding spirochetes in an aneurysm of the abdominal aorta. He has accomplished this now in 5 cases.

Pneumoperitoneum has been employed by Ribadeau-Dumas and Mallet¹³⁵ as an aid in the diagnosis of abdominal aneurysm. Three such cases are reported.

DISEASES OF ARTERIES.

Arteriosclerosis. Arteriosclerosis is another term for aging writes Norris¹³⁶ in a discussion concerning the etiology and symptomatology of this condition, and he quotes Osler's saying that "The tragedies of life are largely arterial."

Although sclerosis of the arteries is nearly always general, yet in a given case certain organs or systems are the chief sufferers. Norris classes the cases as (1) cardiac, (2) renal, (3) cerebral, (4) peripheral, (5) abdominal, (6) nervous. In the cardiac group either the myocardial, valvular or coronary lesions may predominate. "In the cerebral type one finds not only a loss of mental elasticity, an inability to concentrate attention or to enjoy things that once made an appeal, but also psychasthenic manifestations, vagaries of conduct or outbursts of excitement in people who had previously steered a straight course and kept an even keel. One also encounters amnesias and temporary failure, either partial or complete, of vision, hearing or consciousness; also aphasias." Under the heading of Peripheral Sclerosis, Norris states that this type "chiefly is exemplified by vascular spasm, intermittent claudication, spontaneous cramps, neuritic pain as in erythromelalgia, localized gangrene, etc." He also considers thrombo-angitis obliterans a type of arteriosclerosis. This wide application of the term arteriosclerosis has certain advantages.

Ophüls¹³⁷ in an attempt to obtain data concerning the relation of arteriosclerosis to preceding infectious diseases has studied a series of 500 consecutive necropsies of cases which had been thoroughly studied clinically. He points out that because certain infectious diseases are

¹³² Lancet, 1920, i, 1314.

¹³³ Journal of Medical Research, 1920, xlii, 49.

¹³⁴ Bull. d. l. Soc. d. hôp. de Paris, 1921, xlv, 192.

¹³⁵ Ibid., 1920, xlv, 1348.

¹³⁶ American Journal of the Medical Sciences, 1920, clix, 815.

¹³⁷ Journal of the American Medical Association, 1921, lxxvi, 700.

likely to involve the arteries acutely it has been assumed that they might also be concerned in the production of chronic arterial disease. Rheumatic infections and typhoid fever have been most prominently mentioned in this connection, and occasional infections of the arteries have been credited to pneumococci, gonococci and other bacteria. At the same time the results of diphtheria and tuberculosis have been studied. No altogether acceptable proof, however, have been furnished of this suspected interrelation between certain infectious diseases and the late development of arteriosclerosis or of the syndrome of cardiovascular disease. In the series studied by Ophüls the possible existence of preceding infections was determined both by the clinical histories and by careful anatomical study, the latter being directed especially toward the discovery of old inflammatory lesions in the tonsils, heart valves and other known foci of chronic infection. Ophüls compared those cases in which all history or signs of previous infection were absent and those in which such had been detected with the striking result that chronic arterial disease was almost entirely lacking in those with no evidence of infection and made its appearance early and very frequently in the second group. Apparently this connection does not exist in all infectious diseases, but is fairly well limited to what Ophüls terms "chronic rheumatic (septic) conditions." Evidence indicates that the injury to the arteries usually occurs in early life, and the anatomical lesions seem to develop very slowly and progressively, even after the original infection has become extinct. In chronic pulmonary tuberculosis, arteriosclerosis is very rare, and if one disregards true syphilitic disease of the aorta and of the cerebral vessels, arteriosclerosis is apparently rare in syphilis, especially if one deducts those cases in which a chronic rheumatic infection was also present.

Studies in comparative pathology should always be welcomed. Fox¹³⁸ reports the results of an analysis of the arterial findings in 5464 autopsies on wild animals. He includes under the term *arteritis* both productive *endarteritis* and degenerative *arteritis* or *arteriosclerosis*. Among the 5464 examinations only 86 instances were discovered: that is, about 1.5 per cent. It was found most often in cats, dogs, bovines, predatory birds, parrots, gallinaceous and aquatic birds, and in these groups it is most definitely developed in those living on a protein diet. The lesion is very common in the orders showing the greatest number of cases of gastro-enteritis; this is especially true of parrots, aquatic birds and herbivorous and carnivorous mammals. The aorta is more affected in mammals; the disease is more distributed in birds. The animals most affected are those prepared by Nature for severe or prolonged physical effort, such as in fight or flight. These figures are interesting, although taken by themselves it is difficult to draw any immediate conclusions concerning the etiology of human arteriosclerosis from them.

TELANGIECTASIA. By this term is meant a dilatation of capillaries or small venules. On the cheeks, nose and ears they occur frequently

¹³⁸ American Journal of the Medical Sciences, 1920, clix, 821.

in persons exposed to the weather and in heavy drinkers. Scattered telangiectases (spider angiomas) are frequently found in apparently normal persons, but are much more frequent in persons with hepatic disease, jaundice, cancer, syphilis and after exposure of the skin to the roentgen ray. Rarely they occur in a familial distribution. In such instances they are most often found on the skin and mucous membrane of the nose and mouth, less frequently on the tongue, cheeks, lips and elsewhere. They then form what is known as "hereditary hemorrhagic telangiectasia." As a result of these lesions, epistaxis frequently occurs, and they are the underlying cause of the condition of recurring or familial epistaxis. Goldstein¹³⁹ has recently reported 11 cases of this condition in one family. He was able to find only thirty families reported in the literature, which indicates the extreme rarity of the condition. The fundamental fault at present is not known; apparently the blood is normal in every respect and the condition must be clearly differentiated from purpura and hemophilia. It is apparently a fault in the vessels, transmitted from one generation to another, but not according to any known laws of heredity. The resulting hemorrhages may be extremely severe and even fatal. In a recent report by Freudenthal¹⁴⁰ every means to check epistaxis was tried without success. Thromboplastins applied to the nose on a pledget of cotton gave some relief. In the family reported by Goldstein there was a history suggesting that one case had died as a result of hemorrhage.

ABDOMINAL ARTERIOSCLEROSIS. Obliteration or thrombosis of the mesenteric arteries or veins is an important subject and one which is still far from settled. The nature of the process is often uncertain; undoubtedly it is sometimes a true arteriosclerosis. Martinez¹⁴¹ reports such a case in which there occurred paroxysmal pain in the abdomen, with incessant vomiting. The diagnosis of peritonitis from perforation of a gastric ulcer was made, but necropsy revealed obliteration by arteriosclerosis of a group of mesenteric arteries. On the other hand, Ross¹⁴² has recently reported six cases of mesenteric thrombosis representing a variety of different types.

Blood-pressure. **NORMAL.** It is not easy to state exactly what normal blood-pressure is for a given individual. The age, sex, position and other factors all enter into the question. Alvarez¹⁴³ has reported an analysis of the blood-pressure figures in 8737 freshmen at the University of California and in 1000 private patients. The arithmetical mean for women between sixteen and forty was 115 mm.; for men, 126.5 mm. Alvarez concludes from his clinical experience that pressures over 127 in women and over 130 in young men are indicative of hypertensive diathesis which is associated with many typical symptoms and findings. Women before the menopause apparently represent almost exclusively a low pressure type, and they exhibit less variation in the

¹³⁹ Archives of Internal Medicine, 1921, xxvii, 102.

¹⁴⁰ New York Medical Journal, 1921, cxiii, 425.

¹⁴¹ Rev. Espanola de med. y cir., 1921, iv, 69 (abstract, Journal of the American Medical Association).

¹⁴² Annals of Surgery, 1920, lxxii, 121.

¹⁴³ Archives of Internal Medicine, 1920, xxvi, 381.

figures than is true of men at the same periods of life. Alvarez advances the hypothesis that ovarian function may play a regulatory role, keeping the blood-pressure constant, until the ovarian function diminishes or is lost at the menopause.

Another factor which influences the blood-pressure reading is the size of the arm. Hering¹⁴⁴ reminds us that the pressure is always lower in an atrophic arm than in its fellow.

Vasomotor instability as a result of emotion or mental activity may bring about wide variations in the pressure. This is emphasized by Hein,¹⁴⁵ who further states that single blood-pressure estimations often are valueless and that aneroid instruments require frequent checking.

Functional alterations of blood-pressure are described by Ives.¹⁴⁶ Such variations, primarily functional in nature, may be at times hypertensive in reading and in other cases hypotensive. Ives details the various conditions which, according to his hypothesis, bring about these non-organic changes in blood-pressure.

An interesting observation by McKinlay¹⁴⁷ is worthy of note. It was suggested by the occurrence of epistaxis during stomach lavage in a case of arterial hypertension. He then studied the blood-pressure in a series of cases during the passage of the stomach tube and found that there is, as a rule, an increase in blood-pressure of from 20 to 50 mm. of mercury with the passage of the tube. There is a greater increase in those cases in which there is retching, but he believes that the increase is not dependent on straining or mental excitement. In cases of hypertension the percentage increase is greater. It would seem that this might contraindicate the passage of the tube in individuals with severe hypertension and arterial disease.

Crampton¹⁴⁸ has studied with great care the influence of posture on the blood-pressure, and has attempted to draw conclusions concerning the efficiency of the circulation from the changes which are found. The summary of his article is as follows:

1. The horizontal and vertical blood-pressure may differ greatly in the same individual.
2. A rise in systolic pressure on standing indicates efficiency in the gravity-resisting ability of the circulation; a fall the reverse.
3. The increase in heart-rate on standing indicates inefficiency in the gravity-resisting ability of the circulation in proportion to the increase.
4. Taking both influences into consideration an index may be determined for convenient use.
5. This index is lowered by various influences, among which are fatigue, toxins, the approach of disease and disease itself.
6. This index may be high in good health and also in some diseased conditions.

¹⁴⁴ Deutsch. Arch. f. klin. Med., 1920, cxxxiii, 306.

¹⁴⁵ Pennsylvania Medical Journal, 1920, xxiv, 55.

¹⁴⁶ American Journal of the Medical Sciences, 1920, clx, 61.

¹⁴⁷ Journal of the American Medical Association, 1921, lxxvi, 431.

¹⁴⁸ American Journal of the Medical Sciences, 1920, clx, 721.

7. The index may prove helpful in estimating the extent illness is damaging the circulation in the course of disease and in estimating the progress of recovery.

8. This index may indicate the fatigue and the variations of condition in an athlete.

9. The normal range of this value is approximately from 50 to 100, although records in this range may be given by sick persons, but high records in sick persons are probably evidences of pathological overtone.

10. Records below zero are evidences of great lack of circulatory power.

11. Comparison of records of two individuals may or may not give much information. Successive records on the same case may give more.

12. The customary single recording of the blood-pressure in one position gives no information as to the gravity resisting function of the circulation.

HYPERTENSION. An interesting aspect of the question of high blood-pressure has been presented by Quinan¹⁴⁹ under the title "Sinistrality in Relation to High Blood-pressure and Defects of Speech." Sinistrality, or left-handedness, occurs in about 4 per cent of individuals. In addition to the simple form there are crossed forms, in which the left eye may be the master eye in a right-handed person, and *vice versa*. Such crossed forms are usually latent. It has been claimed that sinistrals are more liable to have had difficulties in speech, such as stammering, in childhood. Quinan found in the series of men he studied that as compared with dextrals, or right-handed individuals, stammering occurs in sinistrals with a frequency from three to seven times greater. He also found that high arterial tension occurs more frequently in left-handed than in right-handed people, from which he concludes that in view of the evidence that left-handedness is hereditary a hereditary predisposition is a definite factor in the etiology of high blood-pressure, and that high arterial tension is suggestive of constitutional inferiority.

Another aspect of hypertension is presented by Engelbach.¹⁵⁰ It concerns the relation of arterial hypertension to various endocrine disturbances. This is a difficult subject to discuss at the present time because of the wholly unsatisfactory state of most of the literature on endocrine-gland disturbances. Engelbach, however, is conservative in his conclusions and merely states his findings. Among 500 patients with endocrine disturbances he found 46 who had a systolic pressure of 160 or above. Unfortunately he does not give the diastolic pressure, without which it is, of course, impossible to diagnosticate an increased blood-pressure. The influence of protein food on hypertension is an old question and one which is still under discussion. Mosenthal¹⁵¹ concludes that it is exceptional for a low protein diet to diminish the blood-pressure or a high protein diet to raise it. This, however, may occur, but it is probable that only by a subcalorie diet, maintained for some time, can one hope to materially reduce a raised pressure.

¹⁴⁹ Archives of Internal Medicine, 1921, xxvii, 255.

¹⁵⁰ Journal of the American Medical Association, 1920, lxxiv, 1619.

¹⁵¹ American Journal of the Medical Sciences, 1920, clx, 808.

Large amounts of fluids given to patients with hypertension, and presumably chronic nephritis, may cause a very decided increase in blood-pressure according to Miller and Williams.¹⁵² This may, of course, be dependent upon the promptness with which the kidneys function in excreting water. Dorner¹⁵³ also has studied the influence of water intake on blood-pressure, both in mild and severe nephritis and in non-nephritics. The results are contradictory, and so many factors enter into the problem that no conclusions should be drawn at present.

Vaquez¹⁵⁴ emphasizes the importance of recognizing that the high blood-pressure encountered in such conditions as lead-poisoning and eclampsia may be simply of an acute paroxysmal character. This acute paroxysmal hypertension may, however, be of the utmost importance in the production of other symptoms and results.

DISEASES OF THE LUNGS AND PLEURA.

Respiratory Function. It may be remembered that last year in this article details were given of the claims of Henderson, Haggard and Coburn¹⁵⁵ concerning the value of inhalations of carbon dioxide after anesthesia and operation. Their work was based on the premise that excessive breathing, with blowing off of the carbon dioxide of the blood, reinforced perhaps by diminished carbon dioxide formation in the tissues under anesthesia, leaves the blood abnormally alkaline. In compensation, alkali passes out of the blood, partly perhaps into the urine, but chiefly presumably into the tissues. This is the acapnial process by which a reduction of the all-important blood alkali is claimed to be brought about. By the inhalation of carbon dioxide this process is inhibited and the alkali is recalled into the blood from the tissues. The inhalation of carbon dioxide, according to these observers, brings about an augmentation of breathing which rapidly ventilates the anesthetic out of the blood. Arterial pressure, venous return and possibly intestinal tonus are restored to normal, and a marked decrease of post-operative nausea, vomiting and thirst is evident.

Since that time Henderson¹⁵⁶ alone, or in conjunction with Haggard, has amplified the above conclusions without, however, modifying his fundamental conception of the process. Doubt is cast on the occurrence of an acidosis due to the formation of lactic acid within the body, and the conditions for which this has been offered as an explanation are interpreted in terms of alkalosis—in other words, of a low ratio of carbonic acid to sodium bicarbonate. Under low oxygen supply some respiratory stimulant is produced which Henderson terms respiratory X. This causes not acidosis but overbreathing and alkalosis. Here we seem to come close to the conception of carbon dioxide as the specific respiratory stimulant and the evidence, referred to later, advanced by Jacobs

¹⁵² American Journal of the Medical Sciences, 1921, clxi, 327.

¹⁵³ Deutsch. Arch. f. klin. Med., 1920, cxxxiii, 21.

¹⁵⁴ Paris méd., 1920, x, 433.

¹⁵⁵ Journal of the American Medical Association, 1920, lxxiv, 783.

¹⁵⁶ Journal of Biological Chemistry, 1920, xliii, 3, 15, 29; Journal of Pharmacology and Experimental Therapeutics, 1920, xvi, 11.

in favor of this view. Henderson employs this term respiratory X as an alias for the state of the blood, formerly assigned erroneously to the increase of lactic acid, through which alterations of oxygen tension bring about their effects upon the respiratory center. Apparently respiratory X may, so to speak, be present either to a subnormal or supernormal degree, and depends fundamentally upon the ratio of the oxygen to the blood alkali which in turn is related to the barometric pressure to which one is accustomed to live.

Confirmatory evidence for the above views has come from several sources. For example, Haldane, Kellas and Kennaway¹⁵⁷ reported that the result of the breathing of lowered oxygen tensions, as under conditions of lowered atmospheric pressure, upon the reaction of the urine was a change to the alkaline rather than to the acid side. This fits in with the conception of an elimination of base to keep the reaction of the blood at a constant level, a shift being threatened by the washing out of the carbon dioxide from the blood by the increased breathing resulting from the diminished supply of oxygen in the inspired air.

The use of inhalations of carbon dioxide after anesthesia has met with some opposition and cannot be said to have been at all generally accepted. Van Slyke, Austin and Cullen¹⁵⁸ studied the blood changes in ether anesthesia, and came to the conclusion that even in light etherization the respiratory center is markedly deadened and that the carbon dioxide tension of the blood rises. In deep etherization the carbon dioxide tension rises still higher, but respiration not only fails to be accelerated in response to the increased carbon dioxide tension, but may even be so retarded that the oxygen saturation of the arterial blood falls below that normally found in venous blood. Further findings, which need not be detailed here, lead them to the conclusion that even in light ether anesthesia there exists a state of uncompensated acidosis. In view of these findings it would seem that little benefit could be anticipated from inhalations of carbon dioxide following anesthesia.

Reimann, Bloom and Reimann¹⁵⁹ report unfavorably on the practical use of inhalations of carbon dioxide after anesthesia and operation. They followed out the technic described by Henderson, Haggard and Coburn and studied the results of this procedure both in humans and in dogs. They conclude that the administration of the carbon dioxide to the patients did not materially hasten recovery from the anesthetic and did very little toward preventing vomiting and gas pains. Nothing short of mathematical methods would discover the differences brought about by the carbon dioxide inhalation, if any exist. Determinations of the plasma carbon dioxide before and after the inhalations show that the administration of this substance did not uniformly increase it in the plasma. In fact, it fell in more instances than it rose. They do not deny that the carbon-dioxide carrying-power of the blood is reduced by anesthesia, but this they attribute to the entrance into the blood of other stronger acids which displace the carbon dioxide. In other words

¹⁵⁷ *Journal of Physiology*, 1919, liii, 181.

¹⁵⁸ *Proceedings of the Society of Biology and Medicine*, 1920, xvii, 169.

¹⁵⁹ *Journal of the American Medical Association*, 1921, lxxvi, 437.

it is an acidosis rather than a tendency toward an increased alkalinity which is at work. Under this premise there is no indication for the administration of carbon dioxide; so that from both the practical and the theoretical standpoint they find no justification for its use after anesthesia. They do, however, feel that the administration of base in the form of sodium bicarbonate in a practical way is indicated in order to raise the lowered carbon-dioxide carrying-capacity of the blood to normal. Carter¹⁶⁰ from experimental work on dogs comes to the conclusion that ordinary ether anesthesia causes a distinct decrease in the alkali reserve, but this is an actual decrease and not an apparent condition due to hyperpnea. The greatest decrease in the alkali reserve occurs at the end of the anesthesia and remains level for from one-half to one hour after the termination of the anesthesia, at a time when there is decreased respiratory activity. This is another argument against the overventilation hypothesis and against the usefulness of carbon-dioxide inhalations. Carter is very careful to point out, however, that his experiments on normal dogs must not be too quickly applied to human patients undergoing a surgical operation or in surgical shock.

In reply to the criticisms of their method, Henderson, Haggard and Coburn¹⁶¹ claim that Reimann, Bloom and Reimann did not correctly carry out their original technic, and also that the patients on whom Reimann, Bloom and Reimann made their observations were not suitably chosen, inasmuch as they were returned from the operating room in good condition with good color, warm skin and a fairly regular respiratory rate. These patients, evidently, had not suffered to any appreciable degree that depression of vitality which comes on usually only when anesthesia and operation are prolonged beyond an hour. It is to the relief of such depression that the carbon-dioxide therapy is claimed to be particularly applicable. Henderson and his coworkers ask for a fair trial for the procedure and a judgment based on the results.

RELATION OF TETANY TO ALKALOSIS. It has long been observed that muscular twitchings suggesting tetany may follow overventilation of the lungs from forced breathing, but no satisfactory explanation was advanced. A year ago Grant and Goldman¹⁶² advanced evidence to show that forced respiration may produce the characteristic symptoms of tetany and that these phenomena are probably to be explained as being brought about by the alkalosis which results from the over-ventilation. The well-known carpopedal spasm is produced as well as the reactions to which the names of Erb, Chvostek and Trousseau have for so many years been associated. In the older observations by Vernon, Henderson and by Hill and Flack various similar phenomena had been observed, but their identity with those seen in tetany had apparently not been appreciated. There are some other observations upon tetany produced in other ways which also suggest that alkalosis may be at least one of the important exciting causes of tetany. "Alkalosis" has been observed just before an attack of tetany after the removal of the

¹⁶⁰ Archives of Internal Medicine, 1920, xxvi, 319.

¹⁶¹ Journal of the American Medical Association, 1921, lxxvi, 672.

¹⁶² American Journal of Physiology, 1920, lii, 209.

parathyroids in dogs. The beneficial action of calcium salts in tetany may be due to a relative increase in acid radicals caused by their administration. Clinically, gastric tetany is most liable to occur in those cases in which there is some pyloric obstruction, so that the acid gastric secretion does not reach the duodenum and excite alkaline intestinal secretion, and this might be expected to leave the blood with an excess of basic substances. Experimental work on gastric secretion also suggests this relationship, and cases of tetany following therapeutic administration of sodium bicarbonate have been reported. Also, experimental injections of sodium phosphate have produced symptoms of tetany. Finally, ammonia-poisoning produces symptoms strikingly similar to those of parathyroid tetany.

In the conditions named, as well as following pulmonary overventilation, an "alkalosis" might be expected to occur, and Grant and Goldman consider this of great importance irrespective of the changes in the calcium content of the blood, to which so much attention has been drawn recently. The overventilation may be brought about by voluntary forced breathing or may occur incidental to anesthesia, injury or disease. It is on this basis that the authors explain the tetany which has been reported as following gynecological operations. Why tetany should result from alkalosis, if it does, is not clear, but it has been suggested that the tetany is a means adopted by the body to produce acid products by muscular action in order to restore the temporarily disturbed alkalinity of the blood. Analogy is drawn to the compensatory heat-production by shivering. If this hypothesis is true it would suggest that that type of muscular action seen in shivering is productive of more heat and that the spasms of tetany are more efficient in the production of acids.

The whole conception of alkalosis must still be held *sub judice*, but it is of interest thus briefly to review it as it affects or is affected by respiratory function.

THE STIMULUS TO THE RESPIRATORY CENTER. At different periods various factors have been emphasized, and the older view that the respiratory center responded to the stimulus of an increase in the blood carbon dioxide was temporarily discarded in favor of the theory that the respiratory center is stimulated by a more acid reaction of the circulating blood irrespective of the nature of the acid and that carbon dioxide acts merely in the capacity of an acid. Even more recently the older view has come again into favor, and evidence is being advanced to prove that carbon dioxide has a specific stimulating action on the center. That this specific action may depend upon carbon dioxide being an acid does not in the final analysis alter the specificity of the stimulating quality. Interesting work by Jacobs¹⁶³ is directed as the solution of this problem. Although others have advanced that carbon dioxide has a specific stimulating influence on the respiratory center, no adequate hypothesis for this action had been advanced until Jacob's reports. He has shown that carbonic acid has a much greater power

¹⁶³ American Journal of Physiology, 1920, li, 321; *ibid.*, liii, 457.

of penetrating living cells than other acids. This was conclusively demonstrated in the case of protozoa and plant cells. Experiments with tadpoles evidence the greater toxicity of this acid, even in neutral solution, to these animals than solutions of other acids: hydrochloric, oxalic, salicylic, formic, acetic or butyric of the same hydrogen ion concentration. This toxicity would seem to be explainable only on the ready entrance of this one acid, carbonic, into the cell. Working with the flowers of *Symphytum peregrinum*, which contain a natural indicator sensitive to carbonic acid, Jacobs was able to demonstrate that a condition of intracellular acidity can be produced by a slightly alkaline solution of sodium bicarbonate containing carbon dioxide. The intracellular change in reaction is brought about by the alkaline solution containing carbon dioxide almost as efficiently as by a solution of carbon dioxide in distilled water, though the hydrogen ion concentration of the latter solution is approximately four thousand times as great as that of the former. Thus a very weak acid, carbonic acid, because of its ability to penetrate the cell membrane, can leave the alkaline sodium bicarbonate solution, enter the cell and bring about intracellular acidity. Other stronger acids fail to do this and only enter the cell after a considerably longer period from acid solution. These same results are obtained when an artificial cell is used. Such a cell can be constructed by overlaying in a test-tube a weakly alkaline sodium bicarbonate solution, tinged pink with phenolsulphonephthalein, with a narrow layer of xylene level with the top of the tube. Over this a celloidin film is placed to keep the solutions in place. This artificial cell may be immersed in any desired solution and the development of intracellular acidity observed by the change in the color of the indicator.

The evidence by all these methods agrees, and Jacobs points out that if similar conditions exist in the mammalian respiratory center this hypothesis would reconcile the two apparently conflicting views held at present as to the method in which carbon dioxide acts as a respiratory hormone or stimulant.

ERYTHROCYTOSIS (SECONDARY POLYCYTHEMIA RUBRA), THE PART PLAYED IN ITS PRODUCTION BY DISEASE OF THE HEART AND LUNGS AND BY ALTERED RESPIRATORY FUNCTION. Those who read this article¹⁶⁴ last year will remember that in the brief review on respiration function it was pointed out that one of the responses made by the body to an oxygen-lack is an increase of the circulating erythrocytes or at least such a redistribution of these cells that the count made on peripheral capillary blood shows a considerable heightening. Such a compensatory increase in the erythrocyte count may be of considerable degree, the count rising to at least 7,000,000 or 8,000,000 cells per cubic millimeter. As was said last year, all individuals do not respond to an oxygen-lack by the same method, but this is beyond our immediate interest at this time. In the most easily understood form of oxygen-lack, that due to altitude, the response is quite uniform; there occurs a primary rise in the erythrocyte count which appears so promptly as

¹⁶⁴ PROGRESSIVE MEDICINE, September, 1920, iii, 120.

to make it almost certain that it is due to a redistribution rather than to a new formation of the red cells. Later a secondary and more permanent increase occurs which is probably due to increased bone-marrow erythrogenic activity. The causes of compensatory erythrocytosis or secondary erythremia, as it is sometimes called, are many and various, and some of them cannot clearly be attributed to a lack of oxygen, although many can. In those that can be explained upon an oxygen-lack the majority are related, as might be expected, to disease of the lungs or of the heart. There are certain types of pulmonary disease which seem, however, to have more effect in this direction than others, as will be referred to later.

Santos¹⁶⁵ gives the following list of causes of compensatory forms of polycythemia:

1. Cardiopathic, congenital and acquired.
2. Toxic, arsenical.
3. Pulmonary.
4. Associated with duodenal ulcer.
5. Associated with chronic pancreatitis.
6. Due to tuberculosis of the spleen.
7. Premenstrual.
8. The polycythemia of high altitudes.

Still other causes mentioned by other writers include extensive burns, chronic acetanilide-poisoning, chronic sulphonal-poisoning and various experimental procedures such as artificial compression of the thorax, compression of the superior vena cava and stenosis of the larynx or trachea.

It is difficult to understand the steps by which certain of these causes finally bring about the increase in the circulating erythrocytes. Possibly some of the newer concepts of capillary activity will be found to apply, the partial or complete closure of large capillary beds necessitating a reduction in the total circulating blood, and this being brought about by the removal of plasma from the circulation with a resulting relative increase in the relation of cells to plasma. This would increase the count without postulating any new or increased production of cells. A similar state of affairs exists in those conditions in which a rapid loss of fluid (severe diarrhea, cholera, dysentery) results in a decrease in the plasma and a relative or secondary increase in the cell count.

When we turn to the instances associated with cardiac or pulmonary disease the matter is much simpler; any condition bringing about cyanosis and dyspnea may be causative of an erythrocytosis.

Among the cardiac conditions, congenital lesions and especially congenital pulmonary stenosis, are those which are most liable to result in marked erythrocytosis, although almost any chronic disease may bring about lesser increases; whereas of the pulmonary diseases which result in the most marked changes, emphysema and pneumoconiosis are among the most important; but again it must be noted that any disease of which cyanosis and dyspnea are symptoms will usually show some degree of increase in the red-cell count.

One syndrome which has attained the doubtful dignity of having an individual's name applied to it is known as Ayerza's disease.

AYERZA'S DISEASE. This form of secondary or compensatory polycythemia depends primarily upon an arteriosclerosis of the pulmonary arteries, usually of a syphilitic etiology. It has been chiefly in the Spanish-American literature that this syndrome has been emphasized, but recently Warthin¹⁶⁶ has reviewed the literature and reported a case which he believes is the first to be recognized in this country and to be reported in English. Apparently these cases closely resemble primary true polycythemia, the condition first described by Vaquez and later carefully studied by Osler, in which chronic cyanosis, polycythemia and splenomegaly are the most prominent symptoms.

In 1901 Ayerza, Professor of Clinical Medicine in the National University of Buenos Aires, described the observation that certain of these cases of chronic cyanosis and polycythemia were due to pulmonary sclerosis. Since that time the term Ayerza's disease has been in use as well as the descriptive term "*Cardiacos Negros*," which was employed by Ayerza. Warthin quotes a case reported by Barlaro which was characterized by extreme cyanosis, asthma, intense dyspnea, cardiac hypertrophy, erythremia (red cells, 6,600,000), enlargement of the liver, no demonstrable enlargement of the spleen, Wassermann + + + + and arteriosclerosis of the pulmonary arteries. Barlaro believes that many cases diagnosticated as Vaquez's disease are in reality to be explained as pulmonary arteriosclerosis, and so are in fact instances of Ayerza's disease. In this category he places the first case reported by Vaquez, the case of Parkes Weber and Watson, Vaquez and Laubrey, Saundby and Russell, Osler, Herringham and others. Barlaro believes that not all of the cases are of syphilitic etiology and draws an analogy to Raynaud's disease.

Warthin also quotes from a monograph on this subject by Arrillaga, who believes there can be no doubt as to the existence of a morbid entity called "*cardiacos negros*," characterized by cyanosis, hyperglobulism, dyspnea, cough with expectoration of muco- or mucopurulent sputum, headache, angina hypercyanotica, hemoptysis, vertigo, somnolence, etc. The usual rule is for a period of pulmonary symptoms which may extend over a long time and which terminates in the "*cardiacos negros*" state, which in turn may last from two to five years. Death may result from myocardial failure or from such a complication as bronchopneumonia.

In the differential diagnosis from other forms of cyanosis and polycythemia, Arrillaga emphasizes especially the sequence of the events, the fact that the cyanosis precedes the cardiac failure, the marked hypertrophy of the right heart, the roentgenographic evidence of the dilated pulmonary artery. He also believes that all cases are not syphilitic but, to quote Warthin, "that the lesions in the pulmonary vessels may be secondary to chronic pulmonary disease, bronchitis, tuberculosis, pleural adhesions or any condition producing a final

¹⁶⁶ Contributions to Medical and Biological Research, ii, 1042.

emphysema; or it may be the result of slow infections as syphilis, or malaria, or the result of intoxications."

Warthin's report is too long to detail here, but it may be said that the case had been for several years regarded as an uncomplicated one of "chronic cyanosis with polycythemia (Osler-Vaquez's disease)," with a red-cell count which was as high as 8,760,000 per c.mm. However, Warthin points out that the patient presented the long pulmonary evolution of symptoms in the form of asthma and dyspnea, the later slow evolution of cyanosis, erythremia and secondary symptoms which is characteristic of the Ayerza cases. At the autopsy an extreme atherosclerosis of the pulmonary arteries was found and the microscopic study showed the picture of latent syphilis. On this evidence Warthin feels justified in classing his case as one of Ayerza's syndrome. He concludes that the Osler-Vaquez complex of cyanosis, erythremia and splenic enlargement, is a syndrome having a varied pathology and etiology and is not a specific morbid entity. One group of these cases is primarily due to atherosclerosis of the pulmonary arteries and the symptoms of cyanosis and polycythemia are the result of the deficiency in oxygen supply due to the obstructed pulmonary circulation. Warthin goes so far as to say that probably in all cases of Vaquez's disease in which cyanosis and dyspnea are present the polycythemia is compensatory in nature, for neither of these symptoms belong to a primary erythremia. The cause of the deficiency of oxygen in other cases of Vaquez's disease remains to be demonstrated, and until further evidence is advanced this condition will probably continue to be considered an entity by many writers. The importance of Warthin's point of view is evident, and is a step toward the ultimate analysis of this confusing group of cases.

The conception of this whole group of cases, perhaps belonging fundamentally under the heading of altered respiratory function, is an important one, and even more important than the discarding of the old grouping of these cases with the diseases of the blood and spleen. That we may go so far has not been proved, but it is helpful to consider the possibility and to realize that an oxygen deficiency may underlie all of these cases and that the splenomegaly may prove to be another secondary result.

Parkes Weber¹⁶⁷ does not agree with the views suggested by Warthin. He points out that just as a secondary lymphocytosis, leukocytosis or myelocytosis may be mistaken for true leukemia, so also may a secondary erythrocytosis be mistaken for true polycythemia rubra with splenomegaly, which latter condition he believes is dependent on an apparently primary myelopathic condition (primary hyperplasia of the erythroblastic elements of the bone-marrow). Parkes Weber is unwilling to admit that because very many cases of polycythemia are obviously secondary to known causes, therefore all cases of polycythemia probably are secondary to some cause, although the cause may be as yet undiscoverable. The writer then proceeds to describe certain conditions

¹⁶⁷ British Medical Journal, October 30, 1920, ii, 658.

which, he believes, may be mistaken for true erythremia (primary polycythemia of unknown cause). He includes in this secondary group the so-called polycythemia hypertonica of Geisböck, in which there is hypertension but no splenomegaly. Also the splenomegalic polycythemia rubra which is associated with tuberculosis of the spleen. A third type he describes as "Secondary Polycythemia Rubra (of Longer or Shorter Duration), with Splenomegaly, connected with a Condition of Visceral Blood Stasis of Chronic Thrombotic Origin in the Splenic and Portal Veins." He also includes the type connected with heart disease and the syndrome which bears Ayerza's name. Concerning this latter he states that as an explanation of polycythemia, arteriosclerosis of the pulmonary artery "can occasionally be the correct one, possibly only in exceptional cases." Much more common is a similar picture due to any of a variety of chronic cardiopulmonary conditions. In his experience it is not uncommon for middle-aged individuals, especially Hebrews, who have suffered from long-standing asthma to develop the polycythemia and the picture to which Ayerza applies the term "cardiacos negros." Parkes Weber does not believe that this state of affairs can be related only to one form of cardiopulmonary pathology, nor that it is of necessity always or even frequently associated with syphilis. A feature of some diagnostic importance in these cases is that the cyanosis and erythrocytosis may exist for a long period before the patient's death. Concerning Warthin's case, Parkes Weber writes: "I should regard the so-called erythremia in Warthin's case as an example of chronic cyanosis, with secondary polycythemia rubra of 'cardiopulmonary' origin, on an old syphilitic basis." Parkes Weber points out that cases of what he designates as "Chronic 'Cardiopulmonary' Cyanosis with Secondary Polycythemia Rubra," a group which includes those due to sclerosis of the pulmonary arteries, should not be often confused with typical erythremia (Vaquez's disease). He does, however, believe that it has been done, and instances the two original cases reported in the much-quoted paper by Lucas in 1912. Clinically the obvious signs of disorder of the respiratory system (and clubbed fingers when present), the usual absence of evidence of splenic enlargement to ordinary palpation and the very frequent presence of an enlarged liver (chronic passive congestion) should greatly help to differentiate Ayerza's syndrome from cases of true erythremia. The degree of erythrocytic increase cannot be used in differential diagnosis, for the same high figures may be found in both the primary and the compensatory forms; for example, Parkes Weber quotes counts of between 9,000,000 and 10,000,000 per cubic millimeter in instances of polycythemia secondary to chronic "cardiopulmonary" cyanosis.

It is interesting in connection with this discussion of Ayerza's syndrome to note that Vaquez,¹⁶⁸ in 1892, reported what he then believed to be a case of congenital heart disease with splenomegaly and polycythemia, but which at autopsy, in 1895, turned out not to have any such cardiac lesion and so laid the foundation for the description of

¹⁶⁸ *Compt. rend. Soc. d. biol.*, 1892, xliv, 384.

the syndrome which bears the name of Vaquez. In his first report he refers to a case report by Krehl¹⁶⁹ in which a blood count of 8,104,000 erythrocytes per cubic millimeter and 130 per cent of hemoglobin had been found in a patient who was extremely cyanotic during life, and in whom, at autopsy, a congenital lesion of the pulmonary artery was found. However, on referring to Krehl's original article one finds that in addition to the lesion of the pulmonary artery the patient also had a patulous defect of the interventricular septum.

Miscellaneous Pulmonary Conditions. BOTRYOMYCOSIS. The list of possible causes of disease of the lungs in man is constantly increasing and the importance of some of the less well-known varieties is being better appreciated. McJunkin¹⁷⁰ has recently reported a case which he believes was one of pulmonary botryomycosis. This is a disease better known to veterinarians; its gross lesions consist of abundant chronic granulative tissue, and on microscopic examination "botryomycotic granules" are found. These granules are made up of coccus-like organisms embedded in and surrounded by a hyaline matrix. Human cases have been reported from France, Italy, Switzerland, Africa and Morocco. In this country a case of hepatic involvement was reported, and it is said not to be uncommon in horses. The case reported by McJunkin was that of a four months' old infant who died of what was apparently a bronchopneumonia, perhaps incident to pulmonary tuberculosis. At necropsy, however, the findings strongly suggested a granuloma of the type produced by botryomycosis.

PULMONARY INFARCTION. Postoperative pulmonary complications occurred 55 times in 1562 operations in the records studied by Cutler and Hunt.¹⁷¹ In other words one patient in from every 30 to 50 patients operated on, no matter what the anesthetic, develops a pulmonary complication, and one patient among every 150 to 175 dies from the pulmonary complication. Cutler and Hunt believe that embolism from the operative field is the chief factor in the causation of such complications and that embolism is favored by sepsis, trauma and mobility of the part. Earlier in the year a study of venous thrombosis, pulmonary infarction and embolism following gynecological operations was reported by Hampton and Wharton.¹⁷² They conclude that pulmonary infarction occurs most often in the same class of cases and during the same period of convalescence as femoral thrombophlebitis; that is to say, in cases with some infection and where there has been considerable trauma. Pulmonary infarction may precede pulmonary embolism and usually occurs in the second or third week after operation. It is often not recognized, and is misdiagnosed as a pleurisy because of the pain in the side, friction rub and fever. In the cases studied by these observers the condition had been recognized in only 10 per cent of the cases. This they believed to be due to the fact that the diagnosis has been to too great an extent based on the physical examination instead

¹⁶⁹ Deutsch. Arch. f. klin. Med., 1889, xlv, 426.

¹⁷⁰ Archives of Internal Medicine, 1921, xxvii, 457.

¹⁷¹ Archives of Surgery, 1920, i, 114.

¹⁷² Johns Hopkins Hospital Bulletin, 1920, xxxi, 95.

of on the whole clinical picture. The typical attack of infarction occurs about two weeks after operation, is heralded in by a chilly feeling, with an acute attack of sharp pain in the lower right chest. Two days later a friction rub is heard and later there may develop impairment and changes in breath sounds. A little hemoptysis is not uncommon. By this time the fever is as high as 102° F., but within ten days the whole picture has returned to normal. Occasionally empyema, lung abscess or even gangrene of the lung may follow such an attack of pulmonary infarction.

It seems to the reviewer that these authors draw a distinction between pulmonary infarction and pulmonary embolism, which, clinically, is very difficult to appreciate. This they admit in the general discussion, and define their use of the terms by stating that the difference is one in the size of the embolism, or dislodged thrombus, which enters the pulmonary circulation and which occludes accordingly a larger or smaller vessel. Undoubtedly this difference in size of the occluded artery does divide the cases into two groups with a varying severity of symptoms and radically different prognosis. Their point is well taken that many of the milder groups of cases are not recognized and are diagnosticated as pleurisy.

Infarction depends not only upon thrombosis or embolism of the large vessels, but, as Winternitz, Smith and McNamara¹⁷³ have shown, may be initiated by extensive damage to the capillary bed, as for example by the local necrosis of the alveolar walls which follows intra-bronchial insufflation of acid.

ATELECTASIS. The practical data of atelectasis are summarized by Sewall¹⁷⁴ as follows: (1) A relative degree of atelectasis, partial collapse of the air cells, occurs normally in any pulmonary area which is not habitually undergoing fairly vigorous ventilation; it is favored by feeble and opposed by vigorous inspiratory movements. In proportion as the vigor of respiratory aëration is diminished, the pulmonary collapse becomes more extreme. (2) Collapse may be determined either by compression from without or blocking of the bronchioles within the lung. (3) Lobules of the lung which have recently become airless may by inflation be completely restored to their original condition; but after prolonged collapse, of an indefinite period, organic changes supervene which render them incapable of expansion. (4) Minor degrees of atelectasis may be denoted clinically by the demonstration of circumscribed areas of relative percussion dullness which quickly acquire normal resonance after deep breathing or with change of posture; or by the advent, with deepened breathing, of inspiratory râles which quickly disappear under respiratory exercise. Collapse of an extensive volume of pulmonary tissue is denoted by contraction of the overlying chest wall combined with physical signs simulating those of consolidation or of an encysted pleural effusion. (5) The physical signs of atelectasis owe their diagnostic importance to the fact that they are apt to be developed in just those conditions in which we are justified in expect-

¹⁷³ *Journal of Experimental Medicine*, 1920, xxxii, 211.

¹⁷⁴ *American Review of Tuberculosis*, 1921, iv, 811.

ing the advent of organic lesions whose signs they imitate. Briscoe's¹⁷⁵ work on postoperative massive collapse of the lungs would take us too far afield.

CARCINOMA OF THE LUNG. Cottin, Cramer and Saloz¹⁷⁶ report an analysis of 29 cases of primary pulmonary neoplasm. In 80 per cent the diagnosis was not made; in 19 of the 29 cases there was fever; in 6 there was a coincident tuberculous process. Dyspnea, localized pain and cough were the most constant symptoms. Expectoration was present in two-thirds of the cases, classical currant-jelly clot was found in only 2 cases. Attempts to find tumor cells in the sputum were futile in almost every case in which this was tried. A case of carcinoma of the lung reported by Renaud¹⁷⁷ is interesting because, before the usual symptoms became prominent, there suddenly developed the evidences of obstruction of the inferior vena cava. Death rapidly ensued. At autopsy the primary neoplasm of the lung was found to have been large and to have been limited to the mediastinum.

SYPHILIS OF THE LUNG. Little literature on this subject has appeared during the past year. Gibbs¹⁷⁸ reports on 7 cases with evidences in the lungs of some form of chronic disease, and in which such marked improvement followed antisyphilitic treatment as to justify the view that syphilis was at least in part responsible for the trouble in the lung. Acute syphilis of the lung is reported by Miranda¹⁷⁹ as having been the cause of a rapid destructive process in the lungs of a man, aged nineteen years. No tubercle bacilli could be found, and the Wassermann, which was at first negative, became transiently positive during the course of treatment. Elizalde¹⁸⁰ reviews the great variety of lesions which syphilis may produce in the lungs.

ABSCCESS OF THE LUNG. In this review last year considerable mention was made of the literature concerning abscess of the lung, and emphasis was laid on the frequency with which this complication follows operation on the tonsils, teeth or upper respiratory tract. Brief mention will have to suffice at this time. Porter¹⁸¹ has reported 2 cases in which the pulmonary abscess followed tonsillectomy done under local anesthesia. Porter does not believe that the abscess in such cases can be explained by aspiration, and he is inclined to support the theory of infected embolism from the operative field to the lung *via* the venous return. Peters¹⁸² has reported 7 cases, 5 of which apparently followed pneumonia and tonsillectomy. In 1 case the etiology was uncertain.

HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY. Abscess of the lung is one of the many intrathoracic conditions which may bring about the peculiar changes which are commonly referred to as "hypertrophic

¹⁷⁵ Quarterly Journal of Medicine, 1920, xiii, 293.

¹⁷⁶ Ann. de Méd., 1920, viii, 435.

¹⁷⁷ Bull. d. l. Soc. méd. d. hôp. de Paris, 1920, xlv, 1502.

¹⁷⁸ Southern Medical Journal, 1920, xiii, 788.

¹⁷⁹ Brazil Med., 1920, xxxiv, 675 (abstract, Journal of the American Medical Association).

¹⁸⁰ Ann. d. l. fac. de Med., Montevideo, 1920, v, 315 (abstract, Journal of the American Medical Association).

¹⁸¹ Virginia Medical Monthly, 1921, xivii, 606.

¹⁸² Journal of the American Medical Association, 1920, lxxv, 1060.

osteo-arthropathy." The condition is characterized by enlargement of the ends of the long bones of the hands and feet and clubbing of the fingers. The hands and feet may enlarge, but it is the clubbing of the fingers, curving of the nails and enlargement of the lower ends of the tibia and fibula which are peculiarly characteristic. It is seldom appreciated how rapidly these changes may develop, while it is also important to realize that marked improvement may take place. In the case reported by Butler¹⁸³ great improvement in the osteo-arthropathic condition occurred following the elimination of the infection in the lung. The original abscess had followed a tonsillectomy. In the case reported by Kleinberg,¹⁸⁴ on the other hand, the underlying pulmonary disease was chronic fibrous tuberculosis. The changes in this case are said to be (a) permanent globular enlargement or clubbing of the distal phalanges of the fingers and toes; (b) parrot-beak deformity of the nails of the toes and fingers; (c) subperiosteal deposit of bone along the shafts of the long bones of the extremities, and (d) thickening of the tip of the nose and to a less marked degree of the malar regions. In this last is a hint of the changes which sometimes lead to confusion between this condition and acromegaly—a confusion which dates back to some of the first cases on record in the literature.

FOREIGN BODIES IN THE AIR PASSAGES. Although considerable space was devoted to this subject in last year's review a recent article by Jackson¹⁸⁵ demands attention. It is based upon a study of 789 cases of foreign bodies in the air or food passages and so represents a unique experience. It seems proper to quote verbatim Jackson's summary of the chief points in symptomatology and diagnosis insofar as it concerns the air passages.

Larynx. 1. Foreign bodies lodged in the larynx cause an initial laryngeal spasm which is followed by more or less laryngeal wheezing, croupy cough and a variable degree of impairment of phonation.

2. Pain in the laryngeal region may be present and is sometimes referred to the ears.

3. The larynx may tolerate a thin, flat foreign body for a relatively long period of time, but the development of increasing dyspnea renders early removal imperative in the majority of cases.

Trachea. 4. Tracheal foreign bodies are generally movable and their movements can usually be felt by the patient.

5. The vibrations may be palpated and heard with the stethoscope.

6. Cough is usually present at once, may disappear for a time and recur or may be continuous, and may be so violent as to induce vomiting.

7. Sudden shutting off of the expiratory blast and phonation during paroxysmal cough is almost pathognomonic of a movable tracheal foreign body.

8. Dyspnea is usually present and is due to the bulk of the foreign body plus the subglottic swelling caused by the traumatism of the shiftings of the intruder.

¹⁸³ Journal of the American Medical Association, 1920, lxxv, p. 233.

¹⁸⁴ Ibid., 1921, lxxvi, 435.

¹⁸⁵ American Journal of the Medical Sciences, 1921, clxi, 625.

9. The asthmatoïd wheeze is usually present and is often louder and of lower pitch than the asthmatoïd wheeze of bronchial foreign bodies. It is heard at the mouth but not at the chest wall.

10. Pain is not a common symptom but may occur and be accurately localized by the patient.

Early Symptoms of Irritating Foreign Body (Such as a Peanut Kernel) in the Bronchus. Bronchi.

11. Initial laryngeal spasm is almost invariably present with foreign bodies of organic nature such as nut-kernels, peas, beans, maize, etc.

12. A diffuse purulent laryngo-tracheo-bronchitis develops within twenty-four hours in children under two years.

13. Fever, toxemia, cyanosis, dyspnea and paroxysmal cough are promptly shown.

14. The child is unable to cough up the thick mucilaginous pus through the swollen larynx and may "drown in its own secretions" unless the offender be removed.

15. Lung abscess rapidly forms.

16. The older the child the less severe the reaction.

17. In the early stages an acute obstructive emphysema is present, manifested by: (a) limited expansion, (b) muffled tympanitic percussion note, (c) markedly diminished or absent breathing on the free side.

18. The radiograph confirms these signs by showing (a) greater transparency on the obstructed side, (b) displacement of the heart toward the free side, (c) depression and limitation of the diaphragmatic movement on the obstructed side.

Symptoms of Prolonged Foreign Body Sojourn. Bronchi.

19. The time of inhalation of a foreign body may be unknown or forgotten.

20. Cough and purulent expectoration ultimately result although there may be a protracted delusive symptomless interval.

21. Periodic attacks of fever, with chills and sweats and followed by increased coughing and the expulsion of a large amount of purulent, usually more or less foul material, are so nearly diagnostic of foreign body as to call for exclusion of this probability with the utmost care.

22. Emaciation, clubbing of the fingers and toes, night-sweats, hemoptysis, in fact all of the symptoms of tuberculosis are in most cases simulated with exactitude, even to the gain in weight by an outdoor regimen.

23. Tubercle bacilli have never been found in the bronchoscopic clinic associated with foreign body in the bronchus. It was the only element lacking in a complete clinical picture of advanced tuberculosis. A point of difference was the rapid recovery after removal of the foreign body.

24. The erroneous statement in all of the text-books that a foreign body is followed by phthisis pulmonalis is an heirloom of the days when the bacillary origin of true tuberculosis was unknown, hence the foreign

body phthisis pulmonalis or pseudotuberculosis was confused with the true pulmonary tuberculosis of bacillary origin.

25. The subjective sensation of pain may allow the patient to localize a foreign body accurately.

26. Foreign bodies of metallic or organic nature may cause their peculiar taste in the sputum.

27. Offensive-odored sputum should always suggest bronchial foreign body; but absence of sputum, odorous or not, should not exclude a foreign body.

28. Sudden complete obstruction of one main bronchus does not cause noticeable dyspnea provided its fellow is functioning.

29. Complete obstruction of a bronchus is followed by rapid onset of symptoms.

30. The pleura is rarely involved. Rib resections done for supposed empyema have with one exception shown no pus.

31. The physical signs usually show limitation of expansion on the affected side, impairment of percussion and lessened transmission or absence of breath sounds distal to the foreign body.

32. The "asthmatoïd wheeze" may if present be of great diagnostic value. Its absence, however, does not negative the presence of a foreign body.

33. All cases of chest disease should have the benefit of a radiographic study to exclude bronchial foreign body as an etiological factor, and negative opinions should never be based upon any plates except those of the utmost perfection that the wonderful modern development of the art and science of roentgenology can produce. In doubtful cases the negative opinion should not be conclusive until a roentgenologist of long and special experience in chest work has been called in consultation. Even then there will be an occasional case calling for diagnostic bronchoscopy.

34. Symptoms of pulmonary abscess or other lung disease, even cough, following within a few weeks of the extraction of teeth call for the exclusion of a foreign body in the lung.

Notes on Diagnosis. SIGNIFICANCE OF LOWER THORACIC PHLEBECTASIS. The dilated capillaries which are so often seen on the lower thorax and upper abdomen, and which sometimes are numerous enough to warrant the name "capillary girdle," are familiar to all examiners, but there is a wide difference of opinion as to the significance of this finding. Morgan¹⁸⁶ has reviewed this subject thoroughly. He observes that it is vastly more often seen in men than in women; it is more frequent after the age of thirty. Of 100 cases in which such dilated capillaries were observed, 95 were men and 5 were women. The heart was normal in 78 cases and diseased in 22; the lungs were normal in 91 cases and diseased in 9; the liver was normal in 71 cases and diseased in 29. Other possible factors were even less evident in the statistics. Morgan concludes, from his study, that it was impossible to discover the exact determining cause or causes for the condition. It is an accompaniment

¹⁸⁶ Journal of the American Medical Association, 1920, vol. lxxiv, 1694.

of more or less profound pathological changes of the mid-body, and is without doubt associated most often with disease of the liver, heart or the great vessels.

RUBBER-BALL SOUND AFTER COUGH has been claimed to be a sign of cavity, and Bergmark¹⁸⁷ claims to have observed it in almost every case of cavity in the lung. It may also occasionally be produced by adhesions of the pleural layers; in fact, he found it in 4 of 47 cases of pleurisy.

DIAGNOSIS OF DIAPHRAGMATIC HERNIA AND EVENTRATION. This is a subject which needs to be clarified; the ambiguous use of terms has led to much confusion. For instance a case has recently been reported by Portis and Portis¹⁸⁸ under the title of Diaphragmatic Hernia. The authors emphasize the importance of distinguishing between eventration and hernia, and they quote the points of differential diagnosis according to roentgenological findings. The distinction which they claim is not easily appreciated, nor does their case report seem to present the evidence which, according to other writers, would permit its being placed in the hernia group. The difficulty is one of terminology.

A very excellent review of our knowledge concerning the diaphragm has recently been published by Funk.¹⁸⁹ He properly emphasizes the importance of the study of the diaphragmatic movements as an aid to the diagnosis of pulmonary and other diseases. The anatomical and physiological relations of the muscle are given and the methods to be employed in its study. The list of conditions which may alter the position of the diaphragm is amazingly long. Concerning diaphragmatic hernia he adopts the usual view and classification. The article deserves to be read in full.

Funk defines eventration as a thinning of the diaphragm, the layers remaining intact and the structure assuming a higher position than normal. On the other hand diaphragmatic hernia occurs through one of the normal openings which has become dilated or through an abnormal opening, and is characterized by the protrusion of abdominal contents into the chest cavity. Acquired hernia is really an evisceration and should be separated from the acute congenital diaphragmatic hernia. The confusion in this subject is evident by a comparison of the above with the case reported by Portis and Portis and with the case reported by Steenhuis.¹⁹⁰ In this latter the translator has referred to a case with a congenital slit in the diaphragm as one of eventration.

DIAGNOSTIC PNEUMOTHORAX. Fishberg¹⁹¹ has utilized diagnostic pneumothorax as a method of diagnosis of intrathoracic neoplasm. Its value results from the clearer discernment of the tumor mass when it is outlined by the air-containing area. The method is not new, but Fishberg claims that the roentgenograms he has obtained are the first

¹⁸⁷ Upsala Läkaref. Förh., 1921, xxvi, 127 (abstract, Journal of the American Medical Association).

¹⁸⁸ Journal of the American Medical Association, 1920, lxxv, 1262.

¹⁸⁹ Medical Clinics of North America, 1921, iv, 1045.

¹⁹⁰ Nederl. Tijdschr. v. Gen., 1921, i, 400 (abstract, Journal of the American Medical Association).

¹⁹¹ Journal of the American Medical Association, 1921, lxxvi, 581.

that show the tumors clearly. He was led to use the method by the clear roentgenographic demonstration of a mediastinal tumor, which was observed after a pneumothorax had been accidentally produced during the tapping of a pleural effusion. The method is claimed to be harmless, but concerning this the reviewer wishes to withhold judgment. In some instances it would seem that much the same result would be obtained by the removal of the effusion alone without the introduction of any air.

Bronchi. BRONCHIAL FUNCTION has been studied by means of the roentgenograph by Bullowa and Gottlieb.¹⁹² Their experiments were carried out in dogs by the injection into the bronchial tree of opaque substances. Under these conditions a bellows-like action in the trachea and bronchi was observed under the fluoroscope. This action may be limited by contraction of the bronchial muscles. By the action of the bronchial muscles a peristaltic movement is induced which seems adequate to empty the bronchi without the aid of ciliary movement. The lungs can be seen to empty themselves largely by means of this peristaltic movement, and even when the dog is held upright so that gravity, which readily empties a dog's lung, cannot act, successive masses of the injection are seen to be expelled from the larynx and to travel down the esophagus without evidence of accompanying cough. This movement is entirely too rapid to be attributed to ciliary action. These observations are of great interest, in that they help to explain the means by which the lungs rid themselves of overabundant secretion or of fluid materials which may enter the bronchial tree. Cases have been reported in which opaque material passed into the bronchial tree through a tracheo-esophageal fistula was seen injecting the finest radicles, and yet no untoward symptoms developed. Similarly this work is of interest in connection with the therapeutic or diagnostic injection of the bronchi. The ultimate disposition of the injected material being of great importance, therapeutic bronchial injections were made as far back as 1887, and the diagnostic use of bismuth insufflation has been reported by Chevalier Jackson and others. Recently, Lynah and Stewart¹⁹³ have studied cases of bronchiectasis and of lung abscess after direct injection of a bismuth mixture through a bronchoscope. The mixture employed consisted of bismuth subcarbonate in pure olive oil; it is sterilized by boiling.

POSTINFLUENZAL BRONCHITIS, ETC. Last year in this review a number of articles were referred to which emphasized the frequency of chronic non-tuberculous lung disease as a sequel to influenza. Radin¹⁹⁴ comes to the same conclusion that tuberculosis following influenza is not common while non-tuberculous chronic lung disease is. It is easy to say "tuberculosis" in such cases, but it is a very difficult thing to prove.

Packard¹⁹⁵ prophesies that on account of the recent high incidence

¹⁹² American Journal of the Medical Sciences, 1920, clx, 98.

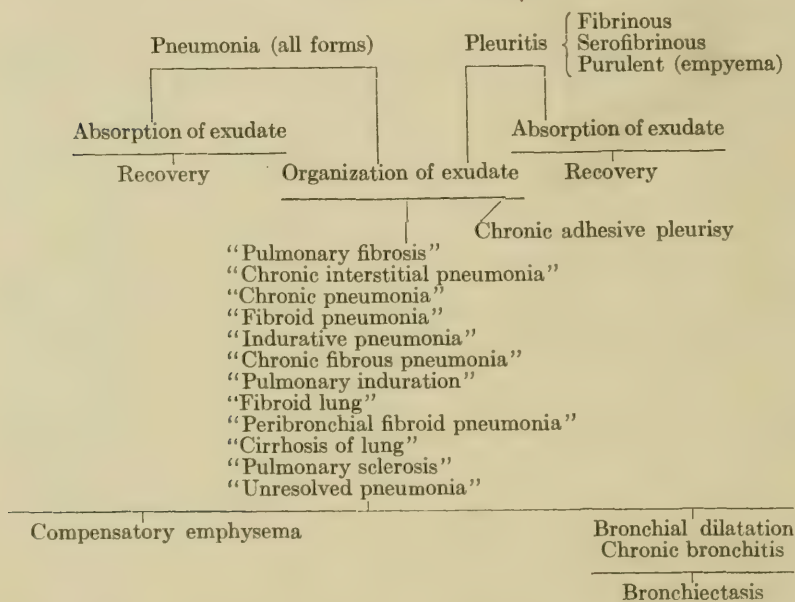
¹⁹³ American Journal of Roentgenology, 1921, viii, 49.

¹⁹⁴ American Journal of the Medical Sciences, 1920, clx, 233.

¹⁹⁵ Journal of the American Medical Association, 1920, lxxv, 1537.

of pneumonia a great many chronic lung changes will be encountered in the next few years. The changes in such cases will almost always be basal and as a result of the overgrowth of fibrous tissue in the lung there will often occur bronchial dilatation and infection, bringing about chronic bronchitis and bronchiectasis. He outlines the sequence of events in a table which is here reproduced:

FIBROUS CHANGES AND THE COMPENSATORY AND DEGENERATIVE
SEQUELÆ OF PNEUMONIA.



ETIOLOGICAL RELATION OF ACCESSORY SINUS DISEASE to bronchitis and bronchiectasis is stressed by Webb and Gilbert,¹⁹⁶ as a result of experience during the recent war. They quote both English and French observations in support of their view. Many cases give no history of nasal disease, denying pain, nasal discharge or any sign suggesting nasal infection; many have been treated over varying periods for pulmonary tuberculosis. The discovery of the chronic infection of the accessory sinuses is almost the rule in cases of chronic bronchitis or bronchiectasis, and improvement follows the treatment of the upper respiratory tract focus.

SYPHILIS OF THE TRACHEA AND BRONCHI. Stimson¹⁹⁷ gives a *resume* of the diagnostic features of this condition and reports 3 cases. His summary is as follows: In syphilis of the trachea and bronchi the characteristic symptoms are those of the tracheal or bronchial obstruction; that is (1) a peculiar type of dyspnea, with labored, prolonged inspiration and shorter easier expiration; (2) paroxysms of excessive dyspnea,

¹⁹⁶ Journal of the American Medical Association, 1921, lxxvi, 714.

¹⁹⁷ American Journal of the Medical Sciences, 1921, clxi, 740.

sufficient to cause syncope or even death; (3) cough, which is usually hard, brassy and paroxysmal, though quite variable in character; (4) stridulous sounds, particularly during inspiration; (5) frequently an inspiratory sinking-in of the tissues of the root of the neck, epigastrium and lower intercostal spaces; (6) other features, such as more or less profuse sputum, a limitation in the mobility of the larynx, etc. Wide variations from this symptom-complex, however, are not uncommon.

Bronchial Asthma. ETIOLOGY. *Sensitization.* Since Meltzer¹⁹⁸ first suggested a relationship between the phenomena of bronchial asthma and those of anaphylaxis as seen in laboratory animals there has been an increasing recognition of the frequency of specific sensitiveness of these patients to a foreign protein as ingested in food, inhaled in the form of pollens, animal epidermal derivatives, organic dust or absorbed from foci of infection. In a large series of cases reported by various observers practically 50 per cent were found sensitive; especially in children the incidence is high (over 80 per cent), while in adults it is increasingly uncommon and rarely develops after the age of forty.

Our knowledge of the exact nature and origin of this sensitization is as yet fragmentary and uncertain. Some, indeed, have made bold to consider it identical with experimental anaphylaxis (Walker¹⁹⁹), but this view has many opponents and a general term such as "allergy" is more acceptable. Freeman²⁰⁰ has recently suggested the name "toxic idiopathy."

A small number of cases are undoubtedly truly anaphylactic in the strict interpretation of that term. Schloss²⁰¹ has shown that guinea-pigs could be sensitized to milk or egg protein by way of the digestive tract by feeding the substance in large amounts and in the presence of gastrointestinal irritation (enteritis). He was also able in sensitized animals to produce an anaphylactic shock by starvation followed by feeding an overdose of the particular protein. The same writer has observed similar phenomena clinically when infants with diarrhea become sensitized to cows' milk during a short period when breast-feeding was interrupted; a second exposure to cows' milk after several weeks resulted in severe anaphylactic symptoms. Schlutz and Larsen²⁰² and, more recently, Schloss,²⁰³ have succeeded in passively sensitizing guinea-pigs to cows' milk by the injection of the serum of sensitive infants. Finally, in the case of Ramirez,²⁰⁴ we have an instance of the passive sensitization of one human being by the serum of another; the patient who had never before shown any allergic phenomena developed, while riding behind a horse, a severe attack of asthma, two weeks after having received a blood transfusion. On questioning the donor it was learned that he suffered from typical asthma due to horse emanations. Another patient who had received blood from the same donor developed no symptoms.

¹⁹⁸ Journal of the American Medical Association, 1910, lv, 1021.

¹⁹⁹ Oxford Medicine, ii, 217 (Oxford University Press, 1920).

²⁰⁰ Lancet, 1920, ii, 231.

²⁰¹ American Journal of Diseases of Children, 1920, xix, 433.

²⁰² Archives of Pediatrics, 1918, xxxv, 705.

²⁰³ Loc. cit.

²⁰⁴ Journal of the American Medical Association, 1919, lxxiii, 73.

So much for the similarities; but there are certain important differences between experimental anaphylaxis and hypersensitivity in man. Rackemann²⁰⁵ calls attention to the fact that the negative phase (anti-anaphylaxis) observed in animals that have survived anaphylactic shock does not occur in man. This may be due to the fact that the shock ordinarily encountered in human beings has not been sufficiently severe. Furthermore, in human sensitization there is the important element of heredity: in nearly 50 per cent of cases there is a positive family history. There are also striking differences between natural and acquired sensitization in man. Natural sensitization is usually multiple and inherited, or rather the tendency to sensitization is inherited, while acquired sensitization is always single and specific. Vander Veer²⁰⁶ cites the findings of Cooke and himself as regards heredity in a series of 621 cases. When both parents are sensitive 67.5 per cent of the children show sensitization, and the crest of the curve of onset time is before the fifth year. If one parent is sensitive, 60 per cent of the children become so, and usually before the fifteenth year. When neither parent is sensitive the height of the onset curve falls between the twentieth and twenty-fifth year.

Piness²⁰⁷ reports on the etiology in a series of 150 cases. His results are in close agreement with those of other observers: 71 cases (47 per cent) gave positive skin tests. There were 33 reactions to foods, 29 to pollens, 27 to epidermal derivatives and 15 to bacteria; 14 of 15 patients under two years of age were found sensitive, as were 30 of 39 under the age of ten. Over the age of thirty only 8 of 45 patients were sensitive, or less than 18 per cent. Piness calls attention to the fact that the sensitization to one protein in early life is liable to be followed by sensitization to other proteins in later years. Food sensitization predominates in children, but in cases developing after the second decade it plays a very minor part.

According to Vander Veer²⁰⁸ pollen asthmas are the largest single group, constituting over a third of all cases. Scheppegegrell²⁰⁹ states that 85 per cent of the pollen cases occurring in this country are due to the pollens of the following botanical groups: (a) the gramineæ, or grasses, chief among which are timothy and June grass; (b) the ambrosiaceæ including the ragweeds, ambrosias, cockle-burs, xanthium and marsh elders; (c) artemisia, or wormwood, of which there are 60 species in the west, especially on the Pacific coast, where they are a common cause of pollenosis (ambrosiæ and artemesia are both members of the family compositæ); (d) chenopodaceæ, including the docks, chenopods and amaranths. To the westward of 100 degrees west longitude it is necessary to test for all four groups, while to the eastward the artemisiæ may be disregarded. Scheppegegrell emphasizes the fact that only the atmospheric pollens count and that the pollens of the insect-pollinated plants such as clover, daisy, golden rod, oleanders and jasmines may be disregarded.

²⁰⁵ Medical Clinics of North America, 1920, iii, 1065.

²⁰⁶ New York Medical Journal, 1920, cxii, 392.

²⁰⁷ California State Medical Journal, 1921, xix, 29.

²⁰⁸ Loc. cit.

²⁰⁹ New York Medical Journal, 1920, cxii, 112.

It is a common observation that patients date their onset of sensitization to an attack of infection of the respiratory tract, suggesting that an inhaled protein may pass unchanged through the mucous membrane of the air passages. Usually the condition is acute: influenza, acute bronchitis, whooping-cough. Luckie²¹⁰ cites 4 cases in which sensitization apparently followed in the course of a chronic respiratory infection. Two of the cases occurred in tuberculous individuals. A woman with a healed apical lesion developed a chronic cough, to which later were added periods of exacerbation and finally asthmatic attacks. Skin tests were positive for cat hair; the banishing of the family cat and a thorough house-cleaning effected a cure. Another patient, suffering with advanced pulmonary tuberculosis, upon being moved into another room of the house became suddenly worse, with sneezing, coughing spells, difficult breathing, expectoration and hemorrhages. It was found that a trumpet vine was in flower just outside of the window. Skin tests using the pollen of the flower were positive in the patient and negative in two controls. After removal of the vine and cleansing of the room the patient became comfortable within twenty-four hours and showed no further allergic phenomena before her death four months later.

Other Etiologic Factors. It has been usual in the past to refer to a number of conditions to which bronchial asthma may be secondary, notably nasal conditions, pelvic disease in women, gastro-intestinal disturbances and the like. The tendency now is to consider them active only insofar as they might be foci of infection. Certainly infection plays a foremost rôle in cases without discoverable sensitization and usually complicates sensitization cases when they have lasted for a time. Chronic bronchitis and sinus infection are particularly common. It is, however, probably going too far to entirely disregard the possibility of a vagoneurosis of other origin, possibly endocrine, possibly reflex, in some instances.

The year's literature contains the usual case reports of cures effected by the correction of nasal troubles (Jensberg,²¹¹ Shambaugh²¹²). Nasal polyps and infection of the ethmoid sinuses are most frequently observed.

Gutmann²¹³ reports an interesting case in which a diseased appendix played a conspicuous part. The patient, a woman, aged thirty-eight years, ten years previously had first had an asthmatic attack after a dose of pyramidon, with a few subsequent attacks, two of which followed the taking of aspirin. Two years before admission to the hospital she had influenza and bronchopneumonia, since which time there was a rapid increase of the asthma with almost daily attacks. Physical examination showed distinct tenderness over the appendix; periceal adhesions were shown by roentgen-ray. Further questioning developed the history of an acute attack of appendicitis about a year before the onset of the asthma, and since that time alternating spells of diarrhea and

²¹⁰ Medical Record, 1920, xcviii, 733.

²¹¹ California State Medical Journal, 1921, xix, 33.

²¹² Surgical Clinics of Chicago, 1920, iv, 599.

²¹³ Presse Méd., 1920, xxviii, 787.

constipation. By pressure over the appendix, Gutmann was twice able to bring on an acute asthmatic attack. A badly diseased appendix was removed under spinal anesthesia. On the day after operation the patient had a mild attack and since that time has been free of symptoms, a matter of several months. Gutmann suggests that the appendix was the button that, when pushed, rang the bell, but the "battery had to be charged."

Hans Curschmann²¹⁴ discusses the possible endocrine origin of some cases of bronchial asthma. The conception is not a new one; as early as 1861 Rokitansky pointed out that the dyspnea observed in thymic conditions was not true bronchial asthma. Curschmann believes that theoretically in a few instances it may be possible to argue that "hyperthymism" by disturbing adrenal activity may cause a vagus preponderance and thus produce a tendency to bronchial asthma. The clinical evidence is, however, quite to the contrary. As he points out the diseases in which thymus hyperplasia is common, such as Basedow's disease and myasthenia, are extremely seldom associated with asthma, while repeated cases of youthful asthmatics examined by the roentgen-ray have failed to show thymus enlargement. Curschmann has twice seen intermitting Basedow's disease with concomitant attacks of bronchial asthma relieved by adrenalin and attended by eosinophilia. In neither case was there thymus involvement. He describes the cases as being "heterotonic," with conflicting signs of increased sympathetic as well as vagal activity, with, however, a preponderance of the vagal element. He has never observed asthma in myxedema. As for the parathyroids, Curschmann and others have observed in children positive Chvostek's and Erb's signs with abortive tetany phenomena in the extremities and attacks of spasmodic dyspnea relieved by adrenalin and favorably influenced by calcium. He suggests that hypoparathyroidism causes a hyperexcitability of smooth as well as striated muscle. The increased sensibility to pilocarpine and eosinophiles in the sputum show these cases to be vagotonics. There is no clinical evidence that there is hypofunction of the adrenals in asthma, nor has asthma ever been observed in Addison's disease. As for the gonads, there is no apparent relation in the male. In women there are cases that are often quite suggestive clinically: the recurrence of attacks with the menses or the onset of asthma and vasomotor phenomena at the climacteric. There is no evidence that the pituitary ever is a factor in asthma.

Bezangon and de Jong,²¹⁵ in a consideration of the relation between asthma and pulmonary sclerosis, object to the common statement that asthma leads to pulmonary sclerosis with emphysema and chronic bronchitis. They believe that the fundamental disease in these patients is a certain degree of pulmonary sclerosis, cicatricial or active, due to various causes, of which tuberculosis is perhaps most common, others being influenza, pneumococcic or streptococcic infections, poisonous gases, etc. This sclerosis, which is always accompanied at a given moment by chronic bronchitis, presents certain paroxysmal crises

²¹⁴ *Deutsch. Arch. f. klin. Med.*, 1920, cxxxii, 362.

²¹⁵ *Presse Méd.*, 1920, xxviii, 885.

(asthma) in its symptomatology in certain individuals with vivid nervous reactivity, with special sensitization for certain toxic irritations, exogenous or endogenous. This nervous reaction is crystallized, so to speak, in the lungs because of the pulmonary disease. The attack is dramatic, the sclerosis hidden, scarcely revealed clinically or by the roentgen ray. The symptom thus predominates over the disease, and asthma, which in a way is only one clinical form of pulmonary sclerosis as seen in allergic individuals, has been considered the cause of all the later results of this sclerosis.

Alexander and Paddock²¹⁶ studied a series of twenty cases of bronchial asthma with particular reference to their reactivity to pilocarpine and adrenalin. The drug tests and the ordinary laboratory diagnostic methods revealed no constantly associated condition, but there were some interesting observations. The most frequent finding was an abnormally increased sensitiveness to small doses of pilocarpine ($\frac{1}{20}$ of a grain), as evidenced by salivation, epiphora, flushing, feeling of warmth and sweating in over three-fourths of the cases, while in half the patients there also resulted asthmatic breathing. This increased reactivity to pilocarpine is an evidence of a state of vagotonia. At the same time a majority of the cases also reacted to adrenalin with an excessive rise in blood-pressure, pallor, tremor, etc. There was a constant relation between excessive adrenalin reaction and a low blood-pressure, while the smaller number of cases with normal or high blood-pressure regularly gave normal reactions. It was also observed clinically that the patients with low pressures and increased reactivity were relieved in asthmatic attacks by 0.25 cc of adrenalin, a smaller dose of the drug than is usually employed. The writers suggest that in subjects with bronchial asthma who are sensitive to adrenalin the increased vagus tone and irritability may be due to a corresponding lack of tone of the opposing sympathetic, which remains sensitive and still able to react sharply to the stimulus, adrenalin. It is possible that a lack of balance predisposes these patients to the excessive reactions which form the presenting symptoms of bronchial asthma. A striking feature of this series of cases is the frequency with which the same individual showed abnormal irritability of the two opposing divisions of the involuntary nervous system as indicated by the response to the test drugs. This peculiarity is not confined to bronchial asthma, but occurs in such conditions as D. A. H., functional gastric conditions, etc. A further evidence of vagotonia in asthma is the presence of an exaggerated oculocardiac reflex as observed by Lian and Cathala.²¹⁷

Diagnosis. There are few conditions in which it is as extremely important to have a complete detailed history as it is in bronchial asthma. The history of the attacks must include their season and time, the relation to extraneous factors such as foods, contact with animals or their epidermal products, the geographic locality in which attacks occur, even to the room of the house. The historian must inquire into every ramification of the patient's life, his occupation and activities.

²¹⁶ Archives of Internal Medicine, 1921, xxvii, 181.

²¹⁷ Paris Méd., 1920, x, 370.

The physical examination must be the most thorough and searching, with special attention to possible foci of infection, and invoking the assistance of special skill and method (rhinologist, roentgen ray). The sputum must be studied macroscopically, microscopically and by culture.

There are several interesting case reports that illustrate the relation of occupation to asthma. Peshkin's²¹⁸ patient, a druggist, developed bronchial asthma in the winter of 1919, the attacks occurring only when he was at work in his drug store. Skin tests were made using the drugs that occur in powder form and positive reactions found for Dover's powder and for ipecac. Ipecac by the mouth gave no symptoms, but inhalation of the powder produced coryza and typical bronchial asthma. Rosenbloom's²¹⁹ patient, a baker, was found sensitive to rye and to wheat globulin. Gerdon²²⁰ reports eight cases of asthma in fur dye workers, due to sensitization to dyes of the ursol class, made from p-phenyl-diamin, a substance also used in hair dyes. The asthmatic attack does not occur until from a half-hour to twenty-four hours after the inhalation of the ursol dust, which is almost tasteless and odorless to normal persons, but is promptly recognized by sensitive individuals. On changing to another occupation the patients had no further asthma, but it returned on resuming the work, in one case after an interval of seven years. A young woman who had been assisting Gerdon in his chemical experiments with the dyes developed an attack of asthma several weeks later while wearing a fur tippet recently dyed with ursol.

The diagnosis of asthma in childhood presents difficulties, since the symptomatology is not as clear as in adults and the condition may be simulated by other diseases such as chronic bronchitis, whooping-cough, reflex cough due to mediastinal (thymus) growths, foreign bodies in the larynx, bronchi, lungs, ear or esophagus. Mason²²¹ describes four types of cases: (a) Frequent coughing spells which vary in duration and frequency—this type is very common in infants; (b) frequent attacks of bronchitis not associated with any rise in temperature; these two forms are rarely recognized as true asthma; (c) true spasmodic attacks of bronchial asthma with freedom from symptoms in the interval; (d) a constant asthmatic state.

Skin Tests. There is yet much discussion as to the technic of election, intracutaneous or cutaneous. It is claimed by many that the intracutaneous test is too delicate and may at times give false positives. On the other hand it may detect a sensitization that goes unrecognized by the cutaneous method. There is one objection to the intracutaneous procedure that must, however, always be kept in mind: in an extremely sensitive individual it may precipitate a general reaction with serious or even disastrous results.

A case in point is reported by Gerstenberger and Davis.²²² The patient, aged eighteen months, had been weaned at three weeks. At

²¹⁸ Journal of the American Medical Association, 1920, lxxv, 1133.

²¹⁹ American Journal of the Medical Sciences, 1920, clx, 414.

²²⁰ Zentralbl. f. Gewerbhygiene, 1920, viii, 188 and 201.

²²¹ New York Medical Journal, 1920, cxii, 399.

²²² Journal of the American Medical Association, 1921, lxxvi, 721.

seven months there developed an eczema that has continued irregularly since then. Tests at the age of seventeen months by the cutaneous method were negative. A month later the child showed asthmatic symptoms, and it was decided to repeat the tests by the intracutaneous method. The injections were followed by cyanosis that rapidly became severe, and with extreme dyspnea. There resulted a wheal the size of a quarter dollar at the site of injection of the egg-yolk and egg-albumen. Relief was obtained after the administration of adrenalin, a total of 1 cc being required. Some days later the test was repeated and again a severe reaction followed that required 2 cc of adrenalin to control, and the opinion was expressed that the child would probably have died if adrenalin had not been at hand. *The intracutaneous test should therefore never be performed unless one is prepared to give adrenalin for an emergency.*

Bezançon and de Jong²²³ in a discussion of the diagnostic value of sputum examination in asthma state that the occurrence of crystals and spirals is negligible. The finding of eosinophils is, however, of the first importance. Thus their presence proves that spasmodic coughing, especially at night, and the dyspnea in the tuberculous, not explainable by the extent of the lesions, are in fact the result of asthma. They believe also that the absence of eosinophilia excludes in others the assumed asthma and helps separate the cases of dyspnea due to cardiac or renal disease. The sputum is stained by the hematoxylin-eosin method after fixation by methyl alcohol. Freilich²²⁴ calls attention to the common occurrence of overlooking the association of asthma and tuberculosis. There is no antagonism between asthma and pulmonary tuberculosis: consumptives get asthma and asthmatics become consumptive. He reports 36 cases of asthma in which tubercle bacilli were found in the sputum. In one dispensary in a group of 49 tuberculous cases with positive sputum there were 6 asthmatics. He quotes Loca who found 500 tuberculous of 700 asthmatics and Pottenger who found 7 asthmatics among 75 tuberculous individuals. The occurrence in an asthmatic of a rapid pulse, loss of weight, pain in the chest, night-sweats and hemoptysis should strongly suggest the added presence of a tuberculosis.

Bana²²⁵ reports an interesting case illustrative of the simulation of asthmatic attacks by other conditions. The patient, a man of fifty years, residing in Bombay, India, was seized at night with a sudden severe attack of dyspnea without evidence of cardiac or renal disease and without elevation of temperature. The administration of adrenalin and the use of potassium iodide, saltpetre and belladonna gave no relief. The explanation was found when examination of a blood smear showed heavy infestation with filaria, the periods of dyspnea corresponding to the congregation of the parasites in the pulmonary circulation.

²²³ Bull. de l'Acad. de méd. de Paris, 1920, lxxxiv, 253.

²²⁴ Bulletin of the Chicago Municipal Tuberculosis Sanatorium, November, 1920.

²²⁵ British Medical Journal, 1920, i, 796.

Treatment. Gottlieb²²⁶ discusses the principles of treatment. In the first place all infectious foci must be adequately treated, including the nose and sinuses, teeth and tonsils, a diseased appendix, gall-bladder or prostate and pelvic infection in women. The bacteriology of nasal and bronchial secretions, of pus from tonsils or tooth-sockets and of the stool should be studied. The stool may show a marked shift from the normal flora, and in such cases Gottlieb recommends skin tests, using suspensions of the organisms recovered. In this way he has discovered a case of sensitivity to a bacillus of the colon group. When a patient is found sensitive to a food it may be omitted from the diet or the patient desensitized by the feeding of gradually increasing amounts. If an individual be sensitive only to lactalbumin of milk then the milk should be boiled, coagulating the lactalbumin which rises to the top, which may be skimmed off. A person moderately sensitive to wheat can safely take toasted bread and puffed wheat. A baked potato cannot provoke a reaction.

If there is sensitization to an animal epidermal protein, such as feathers, cat hair, etc., then the most satisfactory results are obtained by avoiding contact with the offending substance. Should this not be feasible for occupational reasons then desensitization may be carried out by injection of ascending doses of the protein and the patient should stop his work for the period of treatment. A person sensitive to horse-dander in dilutions under 1 to 500 needs to be desensitized. Such desensitization is not permanent, but must be repeated from time to time as symptoms arise. When a patient is sensitive to bacterial protein, vaccines should be given cautiously and in low dosage in the beginning to avoid severe reactions. When subcutaneous administration yields no results, Gottlieb has given the vaccine intravenously, not oftener than once a week.

Pollen asthma is to be treated by desensitizing injections, or, if the patient's means permit, by going away during the pollen season to a region where the offending plant does not occur. There is no ragweed in Europe and practically none in Canada or the extreme northern parts of this country. As for the vicinity of New York, patients are comfortable on Fisher's Island, Block Island, Fire Island and Beach Haven if there is no land breeze. The grasses are universal in their distribution and can therefore not be avoided. In all desensitizing measures it is essential that the dosage and dilution used be controlled by skin tests.

Drug Treatment is subdivided into that of the attack and of the interval. Most efficacious in the attack is adrenalin. After repeated use, however, it loses its effect. The repeated shock of suddenly raised blood-pressure has baneful effects on the heart and bloodvessels. The drug should never be given intravenously and is not to be used in office practice. The administration of adrenalin in oil, as recommended by Miller to ensure a slower and more prolonged action of the drug, has been tried by Gottlieb, but gave no results. Atropine and morphine

²²⁶ Journal of the American Medical Association, 1920, lxxiv, 931.

may be needed. The iodides and ammonium salts serve to promote bronchial secretion and render the mucus less tenacious. One of the various asthma burning powders may be used, an example of which is the following: Strammonium leaves, 9 parts, potassium nitrate, 1 part. Treatment in the interval is chiefly that of the associated chronic bronchitis.

Gottlieb²²⁷ reports the result of treatment in 31 cases of asthma. Of these 15 were improved, most of them being free of symptoms; the other 16 were unimproved, but some of these had been treated for only a short time.

It is becoming more and more common that patients give themselves adrenalin hypodermically for the relief of asthmatic attacks, and only too often they begin this practice on the advice of a physician. Of course the tendency of the patient is to use the drug far too often, usually at the first sign of discomfort, and in a dosage much in excess of that actually required. As it is, the drug tends to lose its effect and the quantity used mounts the more rapidly. Cases of *chronic adrenalinism* will doubtless be increasingly common. Little is known of the effects in man of the prolonged habitual use of adrenalin. The fatal case reported by Hoxie and Morris²²⁸ is said to be only the second to appear in the literature. Their patient, a woman, aged twenty-four years, had had asthma the year round for six years. During this time the patient had taken an average of 7 cc of adrenalin, usually by hypodermic, and occasionally used morphine or inhalations of chloroform. If deprived of the adrenalin for only a few hours the patient became frantic. Blood-pressure readings were normal. Sudden death occurred about two hours after the last dose of adrenalin. At autopsy the lungs on cut section showed areas of collapsed lung tissue intermingled with areas of emphysema. There was no obstruction along the respiratory tract. The heart which had stopped in systole was a little enlarged and the right side slightly dilated. The openings of the coronary arteries were patent and somewhat sclerotic. The aorta was normal in size, but contained several sclerotic plaques in the ascending portion of the arch. The spleen, liver and kidneys were congested and all the large abdominal vessels were filled with fluid blood. There was thus only very trifling vascular change, the chief finding being the congestion of the abdominal viscera. There were similar findings in Broughton's²²⁹ case, and both agree with the experimental findings of Erlanger and Gass.²³⁰ They found that in animals there resulted circulatory failure due to extreme slowing of the blood through vasoconstriction, with resultant overfilling of the abdominal vessels, especially the veins draining the intestinal tract.

Benzyl Benzoate has been variously recommended for the treatment of asthma, both in the attack and in the interval, also for such conditions as renal and biliary colic, whooping-cough, dysmenorrhea and hypertension, based upon its supposed relaxing effect in smooth muscle

²²⁷ Journal of the American Medical Association, 1920, lxxv, 814.

²²⁸ Endocrinology, 1920, iv, 47.

²²⁹ Journal of the American Medical Association, 1919, lxxiii, 1912.

²³⁰ American Journal of Physiology, 1919, xlix, 345.

spasm. Clinical experience has been variable and in the main not as satisfactory as was expected. More recently the work of Mason and Pieck²³¹ has raised serious doubts as to the efficiency of benzyl benzoate as an antispasmodic for the intact uterus, intestine, stomach and bronchi. They injected amounts much larger than the ordinary therapeutic dose intravenously into dogs, with almost totally negative results on both untreated and previously excited organs, while adrenalin under the same conditions in a dosage of 0.5 cc of a 1 to 10,000 solution gave prompt results. Fall in blood-pressure after large doses of benzyl benzoate was found to be due to a lessened force of the heart-beat. In a recent editorial²³² in the *Journal of the American Medical Association* it is suggested that in judging clinical results with the drug, allowances must be made for impressions, reflex influences and the psychic state of the patient. Woloshin,²³³ however, reports a case in which oral administration of benzyl benzoate failed, but the hypodermic use of the drug in 20-minim doses every three hours and 10 minims of digalen every four hours gave relief. Adrenalin, atropine and morphine had proved of no avail.

Le Clerc²³⁴ reports 2 cases of asthmatic attacks in two boys, aged ten and fourteen years, who were relieved by several five-day courses of daily injections of $\frac{1}{3}$ to $\frac{1}{2}$ grain of emetine.

Hutcheson and Budd²³⁵ report their results with autogenous vaccines in 81 cases of asthma. Twenty-five per cent were not benefited. Seventy-five per cent were definitely improved or wholly relieved, the longest period of relief being three years. In this connection the reviewer wishes to emphasize the importance of the proper preparation of a sputum vaccine. The sputum should be studied in stained smears to get an idea of the types of organisms and their relative prevalence as a guide to relative amounts of organisms recovered on culture to be included in the vaccine.

Adkinson and Walker²³⁶ studied the types of streptococci in the sputum as occurring for several months in two winter seasons that differed materially as to the weather conditions. The same strains prevailed throughout.

A number of years ago Auld²³⁷ recommended the use of peptone in the treatment of asthma. It had been found by Dale that if a guinea-pig were sensitized to several antigens simultaneously and an anaphylactic reaction was subsequently induced by a fairly large dose of one of the antigens, the animal might thereby be rendered refractory to the other antigens. Auld used peptone (Armour) in 0.3 gram doses dissolved in 5 cc of distilled water, given subcutaneously for two doses at three- or four-day intervals, then two doses of 0.6 gram each, finally two injections of 1.0 gram in 7 to 10 cc of water. There is no

²³¹ *Journal of Laboratory and Clinical Medicine*, 1920, vi, 62.

²³² *Journal of the American Medical Association*, 1921, lxxvi, 1252.

²³³ *New York Medical Journal*, 1920, cxii, 403.

²³⁴ *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1920, xxxiv, 802.

²³⁵ *Virginia Medical Monthly*, 1920, xlv, 281.

²³⁶ *Journal of Medical Research*, 1920, xli, 457.

²³⁷ *British Medical Journal*, 1917, i, 581.

constitutional and little or no local reaction. More recently he reports some results of treatment.²³⁸ The cases fall into two groups: (1) Cases in general good health, with a limited duration of the disease, with little family predisposition, with regularity in the recurrence of attacks and freedom from bronchitis and emphysema; these cases gave good results, with considerable or complete relief. (2) Cases with chronic bronchitis and developed emphysema, presenting varying degrees of cyanosis; these are usually cases of long duration, often since childhood and nearly always with a positive family history. These cases were not helped. Auld cites no figures as to the number of cases so treated or the percentage of cases in the two groups.

Ascoli and Fagioli,²³⁹ in view of the favorable results obtained by various observers in the use of pituitrin in bronchial asthma, tried the use of stimulating doses of roentgen ray to the pituitary.

They rayed three fields, one frontal and two temporal, at weekly intervals. Of 5 cases so treated, 1 was unimproved, 1 showed slight improvement and 3 were much improved after three to five treatments. No other forms of treatment were used at the time. It is significant, however, that all cases had their asthma in the winter time and the dates of improvement fell in the months of May and June.

Tuberculosis. The intensive study of tuberculosis which is being made in various quarters today results in the application of every known method to the investigation of some phase of the disease. Many of these studies are isolated pieces of research and the time has not come when they can all be correlated together.

METABOLISM IN TUBERCULOSIS. McCann and Barr²⁴⁰ have found that the basal metabolism of tuberculous patients may be normal or very slightly above that of normal individuals of the same size. The variations above or below normal were very small; further increases in metabolism occur, however, with a rise of body temperature. This tendency to an increased metabolic rate is sometimes offset by the reduction in metabolism which is incident to the patients' loss of weight. In other words the food requirements of tuberculous patients are not large, either as regards total energy value or nitrogen content, and these authors conclude for this reason that forced feeding is unnecessary and may even be harmful in the active stages of pulmonary disease. These investigators suggest that during periods of activity of pulmonary tuberculosis the diet need not contain more than 500 calories above the 2000 to 2500 calories of the basal requirement, nor more than 60 grams of protein. These are much lower figures than formerly were often given and are more in accord with recent clinical experience. An interesting editorial on this matter presents further aspects of the subject.²⁴¹ Woodcock and Ruston,²⁴² on the contrary, have concluded that tuberculous patients require more food than the average amount needed by the ordinary laborer outside. The minimum diet should contain 3500 calories and the diet must be rich in protein and fat.

²³⁸ British Medical Journal, 1920, i, 567.

²³⁹ Endocrinology, 1920, iv, 567.

²⁴⁰ Archives of Internal Medicine, 1920, xxvi, 663.

²⁴¹ Journal of the American Medical Association, 1921, lxxvi, 592.

²⁴² Lancet, 1920, ii, 842.

VITAL CAPACITY of the lungs in pulmonary tuberculosis has long interested investigators. Dreyer and Burrell²⁴³ have emphasized the usefulness of the method in estimating the quantitative measure of the disease process. In some ways the changes in an individual's vital capacity are of more value for prognosis and for the appreciation of the results of treatment than are the physical signs found over the lungs. Of course it is only by comparison of the figures obtained in the patient with the figures for a comparable normal individual Wittich, Myers and Jennings²⁴⁴ have come to similar conclusions. The method will aid in the accurate classification of the cases and in determining the progress of the disease and the influence of treatment.

COMPLEMENT-FIXATION REACTION in tuberculosis may be carried out with the same technic as the Wassermann except for the antigen employed. Watkins and Boynton²⁴⁵ employed the so-called "Miller" antigen, which was prepared from a tubercle mass containing eight strains. They report on 6500 reactions and conclude that the reaction is specific for tuberculosis. The positive reaction can be interpreted as indicating tuberculosis, either active at the time or recently active. The focus may or may not be of clinical significance, which fact must be determined by other means. A negative reaction indicates either absence of infection, excessive activity of the disease, exhausting the antibody, or arrest of the disease with spontaneous disappearance of antibody no longer required.

Apparently the test offers the clinician little certainty at the present time.

Hollaender²⁴⁶ has described a serum reaction which takes place when tuberculin is added to the serum of certain persons. He believes the resulting reaction is due to specific antitoxin in the serum. In other words this reaction reveals the natural reaction to the toxin of the tubercle bacillus. He considers the test of great help in prognosis and treatment.

A CHEMICAL FACTOR IN RESISTANCE TO TUBERCULOSIS is suggested by Corper, Gauss and Rensch.²⁴⁷ In 1889 Weber reasoned that a deficiency of carbon dioxide in the body favors tuberculosis while an accumulation retards the disease. This empiric conclusion is thought to be highly significant by the investigators named above. They found that 3 per cent carbon dioxide inhibits the growth of tubercle bacilli in the test-tube and 15 per cent is "tuberculocidal." Cultures of tubercle bacilli buried in the tissues of animals and permitted to acquire the carbon-dioxide concentration of the body were definitely inhibited in their growth. One must be very cautious in deducing facts of practical value from these suggestive results.

EXPOSURE TO TUBERCULOSIS. Calmette²⁴⁸ points out that every one is exposed from a very early age to infection with the tubercle

²⁴³ *Lancet*, 1920, i, 1212.

²⁴⁴ *Journal of the American Medical Association*, 1920, lxxv, 1249.

²⁴⁵ *Ibid.*, p. 933.

²⁴⁶ *Ztschr. f. Tuber.*, 1920, xxxii, 257.

²⁴⁷ *Journal of the American Medical Association*, 1921, lxxvi, 1216.

²⁴⁸ *International Journal of Public Health*, 1920, i, 3 (abstract, *Journal of the American Medical Association*).

bacillus, and that this exposure is unavoidable under existing social conditions. He therefore urges that children be kept under careful supervision and that tuberculin tests be made every six months in order that any infection may be promptly recognized and treated, and that, if possible, the source of the infection may be eliminated.

Perhaps the greatest degree of exposure to tubercle bacilli is offered by the mate of a tuberculous husband or wife. Ward²⁴⁹ found 91 out of 156 such mates were tuberculous—16 were suspect and 49 were negative. Ward concludes that the majority of the mates of tuberculous husbands or wives do sooner or later show signs or develop symptoms of tuberculosis, but the great majority of the infected recover. Minnig²⁵⁰ last year reported conjugal tuberculosis present in 8.7 per cent of 502 dispensary cases who were married.

Rogers²⁵¹ concludes that other factors are necessary for the development of clinical tuberculosis besides the presence of the organism. In all probability there must be a lowering of the individual resistance power, and as a corollary to this the elimination of clinical tuberculosis from adults will largely depend on the keeping up to normal of the powers of individual resistance.

It would not be proper to emphasize the spread of tuberculosis by direct contact without referring to the other avenues of entrance which may be even more important. Opie²⁵² has reported on the infrequency with which healed tuberculosis of the mesenteric glands is seen in this country. In necropsies on 93 children and 50 adults, he found no instance of this condition. On the other hand, in necropsies on 66 young British soldiers examined in France, there were 18 instances of calcified mesenteric nodules. This fits in with other statistical evidence of the relative frequency of primary intestinal infection in the British Isles.

The tonsillar route of infection is stressed by Van Zwaluwenburg and Grabfield.²⁵³ They studied a shadow which they believe represents a thickening of the pleura over the apex of the lung, and its relationship to tonsillar and cervical gland tuberculosis. This shadow occurred in at least 10 per cent of all chest roentgenograms; in 93 per cent of cases showing tuberculous deposits in the faucial tonsils, and in at least 59 per cent of cases with cervical gland tuberculosis. This apical pleuritis was demonstrated in only 11 per cent of cases without tonsillar tuberculosis. It is suggested that the common route of infection may lie through the tonsil and cervical lymphatics to the apical pleura and thence into the lung. This hypothesis offers an explanation for the frequency of apical lesions, the predominance of right-sided lesions, of the pathogenesis of tuberculous pleurisy with effusion and other obscure features of this infection.

²⁴⁹ *British Journal of Tuberculosis*, 1921, xv, 5.

²⁵⁰ *Journal of the American Medical Association*, 1920, lxxiv, 1445.

²⁵¹ *Ibid.*, lxxv, 1690.

²⁵² *American Review of Tuberculosis*, 1920, iv, 641.

²⁵³ *Ibid.*, 1921, v, 57.

TUBERCULOSIS IN CHILDREN AND INFANTS is the subject of a report by Wollstein and Spence.²⁵⁴ They believe that the majority of cases are infected by aspiration rather than by the swallowing of bacilli with the milk or food. Tuberculosis in the very young may become generalized very rapidly; it often terminates in a tuberculous meningitis. Healed lesions were never found in a series of 184 necropsies on tuberculous children.

Masked juvenile tuberculosis is described by Cooke and Hempelmann²⁵⁵ as an important clinical variety. The child has frequent coughs and colds, with or without known exposure to tuberculosis, attacks of unexplained fever, often with afternoon elevations, anorexia, loss of weight and asthenia. Malnutrition, anemia and the evidences of enlarged tracheo-bronchial nodes are noted on examination. There may also be phlyctenular disease or skin tuberculides. The roentgenogram will often reveal, in addition to the enlarged lymph nodes, some unsuspected lesions of varying size in the lung itself. The intracutaneous tuberculin or Pirquet test is usually positive and the authors lay stress on the value of the complement-fixation test, which they claim is positive in three-fourths of the children of over four years of age.

Location of tuberculosis in the lung in childhood has been studied by Vis²⁵⁶ to see if the same rules applied in childhood as apparently do in adult life. At this latter age tuberculosis of the lungs is found at or slightly below the apex, but in childhood Vis claims there is a physiological cause which predisposes the hilum of the lungs to tuberculosis infection, and in addition a comparative immunity to infection at the apex is a result of the greater respiratory excursion and freer circulation in the child as compared with the adult.

Gelatinous Infiltration of the Lung in Childhood is described by Eliasberg and Neuland.²⁵⁷ The gelatinous infiltration is lobar in distribution, develops very rapidly and is preliminary to caseation. It was observed only in infants of less than a year old. They also describe a so-called "epituberculous infiltration" which is not truly tuberculous, although it occurs, as a rule, in infants with tuberculosis; it is more insidious and may recover entirely.

DIAGNOSIS. "The diagnosis of pulmonary tuberculosis, curiously enough, grows more instead of less difficult as time goes on," writes Lawrason Brown.²⁵⁸ He recalls the day when a patient with cough and expectoration and a few fine râles, possibly above the clavicle, was always considered to be suffering from pulmonary tuberculosis. Later, the appreciation of the fact that influenza might produce such a condition led to confusion, and assistance was looked for in the various applications of the tuberculin test. This test has been used less and less and the roentgen-ray study of the lung was introduced. Complement-fixation to various specific tuberculous antigens was next added

²⁵⁴ American Journal of Diseases of Children, 1921, xxi, 48.

²⁵⁵ American Review of Tuberculosis, 1920, iv, 660.

²⁵⁶ Journal of the American Medical Association, 1921, lxxvi, 1156.

²⁵⁷ Jahrb. f. Kinderh., 1920, xciii, 88.

²⁵⁸ American Journal of the Medical Sciences, 1920, clx, 324.

to our armamentarium and helped exclude certain confusing cases. There is still, however, but one pathognomonic sign of pulmonary tuberculosis, and that is the occurrence of tubercle bacilli in the sputum. The sputum should invariably be examined and a first positive report should be checked up by a second examination.

Râles rank next in diagnostic importance. They should be carefully searched for, and especially after cough. Laennec first called attention to the fact that râles are better heard under such conditions. It is even better to have the patient breathe out half or nearly all of his breath, then cough and inhale. The cough must not be too forceful and the muscles must all be relaxed. Pulmonary tuberculosis can occur without râles, and, indeed, fairly extensive deep-seated disease may exist without any or only with most indefinite physical signs. Râles when heard only at the base of one or both lungs should never be considered as due to pulmonary tuberculosis unless tubercle bacilli are present.

The roentgenogram reveals, in a very large majority of cases, much more disease than is revealed by physical signs. Perhaps the term "minimal" is to be preferred to the term "incipient," and this is especially so in roentgenographic studies. In no cases does the roentgen ray help more than in the minimal cases in which one has found, on physical examination, but slight respiratory changes at an apex, but in which the roentgenograph may reveal a well-marked more or less deeply seated parenchymatous lesion.

Miller²⁵⁹ in discussing the problems of differential diagnosis of pulmonary tuberculosis admits that all methods, even including tuberculin tests, sputum examinations, the roentgen ray and complement-fixation tests may fail, and the physician is forced to depend on the development of that clinical sense on the part of the physician, the pursuit of which constitutes much of the fascination of the practice of medicine. There are times when definite signs in the chest and suspicious symptoms may be found by a thorough general examination to be susceptible of quite other interpretation than the temptingly obvious one of tuberculosis. Crockett²⁶⁰ also emphasizes the importance of a general examination, with attention directed toward other parts of the body than the lungs. This is because help is obtained in the diagnosis of tuberculosis from such an examination: for example the hands and fingers, the nails, ears, eyes; all may supply information of value.

Boeri²⁶¹ also draws conclusions from the physical aspect of the individual: the vertical heart, movable ninth or tenth rib, low blood-pressure, tachycardia, etc., are all thought by him to be suggestive.

The fact that the roentgenographic study of the tuberculous lung reveals the extent of the process, but does not give much help in determining the age of the process or the degree of its activity, is well known. Bolle²⁶² emphasizes these points and also the occurrence of cases with

²⁵⁹ American Review of Tuberculosis, 1920, iv, 502.

²⁶⁰ Glasgow Medical Journal, 1920, cxiv, 129.

²⁶¹ Riforma med., 1920, xxxvi, 736.

²⁶² Ztschr. f. Tuberk., 1920, xxxiii, 32.

few symptoms and signs in which the roentgenogram reveals multiple disseminated small foci. In marked contrast to the symptoms and signs in such cases the prognosis is very grave and the process may rapidly spread and bring about a fatal termination.

Garin²⁶³ reports an interesting case in which a primary severe hemorrhagic purpura occurred in a young man and was followed very soon by an acute nephritis which apparently caused death. However, post-mortem examination revealed a generalized miliary tuberculosis which especially involved the kidneys. His explanation that the purpura and arthritic pains were due to toxins incidental to the tuberculosis does not entirely satisfy, but one is reminded of the claims that erythema nodosum is an evidence of tuberculosis. Our knowledge concerning this group of diseases is so incomplete that we are still in the stage of individual case reports.

Bronchopulmonary Spirochetosis. DISTRIBUTION. Two years ago this subject was briefly discussed in this article and reference made to some of the reports which had appeared. At that time the wide occurrence of the infection had not been appreciated, and, in fact, it has only been during the intervening period that the evidence has been forthcoming which makes us realize the prevalence and importance of this condition.

First recognized in 1906 by Castellani²⁶⁴ in Ceylon, it was soon observed in India, West Africa, the Philippine Islands and the West Indies. During the recent war spirochetel disease of the lungs made its appearance in the Italian, Belgian and French Armies, perhaps as a result of the spread of this infection from troops brought to these countries from the tropics. In the Italian Army it was Castellani²⁶⁵ who recognized the affection which he had described previously in Ceylon, while in France it was studied especially by Violle.²⁶⁶ In Belgium, Nolf and Spehl²⁶⁷ described an affection of the respiratory tract which while due to spirochetel infection, yet they believed should be distinguished from the bronchospirochetosis of Castellani and from the bronchitis due to the spirillum described in France by Violle. Some of these cases occurred among the tropical troops but others appeared in Europeans who had never been in the tropics. Cases were soon reported in England and in South America.

In this country fewer cases have been reported in the literature. Lewis²⁶⁸ has recorded one which he suspects may have developed in the United States, but which he observed in a marine on duty in Cuba. Furthermore, the patient has been on duty in France. Fishberg and Kline²⁶⁹ have recently reported a case in New York in a Russian who had been in this country for six years. Salomon²⁷⁰ states that cases have been observed in Missouri and in Ohio.

²⁶³ *Riforma med.*, 1920, xxxvi, 952.

²⁶⁴ *Lancet*, May 19, 1906, i, 1384.

²⁶⁵ *Presse méd.*, July 5, 1917, xxv, 377.

²⁶⁶ *Rev. gén. de clin. et de thérap.*, March 9, 1918, xxxii, 141.

²⁶⁷ *Arch. méd. Belges*, July, 1918, lxxi, 1.

²⁶⁸ *United States Naval Medical Bulletin*, January, 1920, xiv, 149.

²⁶⁹ *Archives of Internal Medicine*, January, 1921, xxvii, 61.

²⁷⁰ *Ann. de méd.*, January, 1920, vii, 53.

ETIOLOGY. The identity of the spirilla or spirochetes found by these various observers and in these various localities is, of course, uncertain. Our knowledge today of this group of organisms is not sufficient for exact classification and identification of all of the members. Included in the group are the well-known *Spirocheta pallida* of syphilis, the *Spirocheta pertenuis* of yaws, the spirochetes of Vincent's angina, of Spirochetosis icterohemorrhagica and of the closely related Weil's disease. In addition there are many less definitely identified, including the *Spirocheta buccalis*. Whether or not all of these cases of so-called bronchopulmonary spirochetosis are due to one strain of spirochete is an open question; it is possible that under a variety of differing conditions different spirochetes might invade the lower respiratory tract and display pathogenic properties. The lack of similarity in the clinical aspects of the cases reported tends to suggest a variety of etiological agents. It is even possible that at least in some instances the spirochetes are merely accidental invaders with little or no relation to the pathological process. A strong argument in favor of the pathogenic importance of the spirochetes is presented by the remarkably curative effect in many cases of arsenic in almost any form.

In the original cases described by Castellani the spirillum was named the *Spirocheta bronchialis* and was described as showing extreme polymorphism. So did the spirochete found by Violle, but Nolf insists on a quite constant form and states that it is easy to differentiate it from the *Spirillum refringens* of Vincent and from the other known spirilla of the buccal cavity. Here the matter must rest at this time, but it is interesting to keep in mind the possibility of some relationship between the mouth spirilla and those invading the lung. In 1910 Rothwell²⁷¹ reported 2 cases in which he believed that Vincent's organism caused or complicated acute pulmonary infection. In the Base Hospital at Camp Meade I studied for some weeks a negro patient who presented a fever curve much like that of relapsing fever; prior to each pyrexial period he would have a marked increase in pyorrhea, and in the absence of all other evidence I was inclined to believe that the pyrexia was indicative of an extension of infection from the buccal cavity and that the mouth spirochetes might be the causative organisms. Browne²⁷² emphasizes the coincident occurrence of numerous spirochetes about the teeth in two cases of bronchopulmonary spirochetosis. He intimates that the morphology of those from the gums was identical with that of those from the sputum, and that these latter were present in sufficient numbers to suggest strongly that they were of etiological importance. The two cases were clinically quite typical.

Another aspect of this subject is suggested by Sinclair.²⁷³ This observer reports the much greater frequency of hemorrhage in pulmonary tuberculosis when Vincent's spirochete is present in the sputum. Of 410 cases examined 256 showed the presence of the spirochete, while in 154 it could not be found. Of the 256 positive cases 182 were cases complicated with hemorrhage, or 71 per cent. Of the 154 negative cases

²⁷¹ Journal of the American Medical Association, June 4, 1910, liv, 1867.

²⁷² Lancet, May 29, 1920, i, 1164.

²⁷³ American Review of Tuberculosis, May, 1920, iv, 201.

56 were cases complicated with hemorrhage, or 36 per cent. In other words, of 238 cases with hemorrhage the spirochete was present in 182, or 76 per cent, and of the 172 cases without hemorrhage the spirochete was present in 74, or 43 per cent.

The possibility that some of these cases were not tuberculous must be kept in mind; nor must we be too certain that the spirochete or spirillum observed was truly the one causing Vincent's angina. It is true that both the spirochete and the *Bacillus fusiformis* are said to have been present in these cases.

In Castellani's first report he suggested the possibility that he was dealing with a bronchial or broncho-alveolar localization of the spirochete buccalis, which term there is no doubt covers many varieties of spirochetes.

CLINICAL ASPECTS. Castellani²⁷⁴ has described two aspects of the affection which he termed bronchospirochetosis. One form is of short duration, from one to three weeks, and greatly resembles an acute bronchitis. During the first few days there may be a fairly high temperature. The more chronic form simulates a chronic bronchopneumonia of long duration, lasting even several years. At times the process takes on a much more active character, with irregular fever, hemoptysis, loss of weight and strength and ending in death. One of the early cases improved very much over a period of a year, but a chronic cough, with blood-spitting, persisted. Castellani used the very descriptive term "hemorrhagic bronchitis" of these cases. He states that all grades of cases are seen between the acute and the chronic forms. Violle also emphasized the hemorrhagic character of the sputum in the cases he observed; it was quite abundant, very homogeneous, mucoid and of a clear, pink color. His cases had been referred to the hospital with very different diagnoses; sometimes for a bronchitis with hemoptysis, sometimes for pneumonia, for incipient tuberculosis, for pulmonary congestion. Often the physician had been deceived by the hemoptysis into making a diagnosis of tuberculosis, but Violle insists on the almost pathognomonic appearance of the hemoptysis in these spirochetal cases. It resembles the juice of the gooseberry and has a brilliant rose color. Other writers have compared it to laked blood. The cough is frequent and especially so at night; it is more or less suppressed and thick, as though the bronchi were plugged with mucus. Upon physical examination very variable signs are found and little diagnostic help can be expected from this quarter. The general condition is good and interesting to note. Violle states there is no fever. Such a picture may persist for years. For example, Vaccarezza²⁷⁵ has reported a case in which there had been recurring hemoptysis during four years without any impairment of the general health.

The absence of fever, which Violle emphasizes, does not agree with the observations of other authors. For example the case reported by Iacono²⁷⁶ from the Dalmatian coast commenced with generalized malaise, dry cough and high fever, which persisted for several days. Fever is also present in the type of pulmonary spirochetosis which goes

²⁷⁴ Presse méd., July 5, 1917, xxv, 377.

²⁷⁵ Rev. de la Asoc. Med. Argentina, April-June, 1920, xxxii, 173.

²⁷⁶ Journal of Tropical Medicine and Hygiene, March 15, 1920, xxiii, 70.

on to gangrene of the lung. Fetid spirillar bronchitis and pulmonary gangrene is the title under which Nolf²⁷⁷ has recently reviewed his experience during the war with this group of cases. He believes that it should be distinguished from the bronchospirochetosis of Castellani and from the bronchitis due to the spirillum described in France by Violle. The evidence in favor of separating these apparently related conditions is quite convincing, but for practical purposes they must at present be grouped together. Nolf and his collaborator Spehl²⁷⁸ observed altogether 11 cases; in 9 the disease attacked men in good health. The onset was sudden, with malaise, headache, muscular pains and chilliness. Cough appeared early in some cases, late in others; in these latter the condition appeared at first rather as a general affection than as a malady of the respiratory tract. Sooner or later, however, the respiratory symptoms became prominent, but even then the physical signs may only be those of a simple bronchitis. Hemoptysis was pronounced in only 1 of the 11 cases; in another there was some rusty sputum. The sputum not only is not hemorrhagic as in other groups of cases, but rapidly becomes purulent and very fetid. The fever is irregular. There is rapid loss of strength and no spontaneous tendency to recover, although treatment with arsenic is successful. Some of Nolf's cases died without developing pulmonary gangrene, but in another instance a case which presented at first the characteristics of a spirillar bronchopneumonia went on to gangrene of the lung and fatal hemorrhage.

It is interesting to compare with the above description a case reported in this country by Fishberg and Kline.²⁷⁹ Their patient, a Russian, had been in this country for six years. He was admitted to the hospital as a case of pulmonary tuberculosis. The fever reached 105° F. There was severe incessant cough, with copious expectoration of foul-smelling, greenish material, at times bloody. The patient was dyspneic and cyanotic. He had been sick for two weeks when admitted to the hospital. The authors suspected pulmonary gangrene, and physical examination revealed definite signs of pathology in the middle third of the right lung. A roentgenogram confirmed this finding. The laboratory examinations included a leukocyte count of 21,000 and a negative complement-fixation test for syphilis. The sputum was found to contain many spirochetes and fusiform bacilli. The patient died a little over a month from the onset of the illness. At autopsy the lungs showed extensive coalescing lobular and bronchopneumonia of both upper lobes and the right middle lobe. In the right lower lobe, associated with consolidation, there was extensive gangrenous ulceration, the ulcerated areas varying in size from several millimeters to a cavity 4 cm. in diameter. In the necrotic and gangrenous areas spirochetes and fusiform bacilli were found in large numbers. The authors feel that the spirochetes were probably of the type Castellani calls *Spirocheta bronchialis* and that they were responsible for the predominantly gangrenous lesions. To the reader there would seem to be considerable resemblance of this case to those described in Belgium.

²⁷⁷ Archives of Internal Medicine, April, 1920, xxv, 429.

²⁷⁸ Arch. med. Belges, July, 1918, lxxi, 1.

²⁷⁹ Archives of Internal Medicine, January, 1921, xxvii, 61.

DIAGNOSIS. In almost every report the diagnosis has rested upon a careful examination of the sputum for the presence of spirochetes, and the discovery of cases has been proportionate to the alertness of those in charge. Undoubtedly the various clinical pictures should be kept in mind and examinations of the sputum for spirochetes made in suspicious cases. Perhaps it is in the chronic cases that recognition is of the greatest importance, for this group of cases seems quite uniformly to have been diagnosticated and treated as pulmonary tuberculosis for varying periods until the correct diagnosis has been made. The success in some cases of arsenic medication makes proper diagnosis all the more important. Furthermore the conditions may be more or less contagious and diagnosis should lead to isolation or at least to measures to disinfect the sputa, etc.

In the diagnosis it is important to remember the presence of spirillæ or spirochetes normally in the mouth. The sputum must be carefully washed free of mouth contamination and the mouth carefully rinsed before expectorating. The material must be spread in a thin layer and some special method, such as that of Fontana, used to demonstrate the organisms. Possibly the gross appearance of the sputum may suggest the condition, but its proof depends upon the actual demonstration of the spirochete. Apparently the laboratory does not offer other assistance; the blood count shows nothing characteristic; in cases of the Castellani and Violle type there is no leukocytosis, while in cases with gangrene the count may be high. No serological method of diagnosis has been brought forward.

TREATMENT. The foundation of the treatment rests on the intravenous use of some organic preparation of arsenic. This is especially important in the fetid and gangrenous cases according to Salomon. In the chronic cases general hygiene is important and good results have been claimed from the use of iodized oil and iodine by the mouth. Violle found that rest, fresh air and nourishing food were sufficient in his cases and that special antispirochetal therapy did not give very brilliant results. On the other hand good results have been obtained with the mixture recommended by Castellani, the formula of which is:

R—Tartar emetic	gr. ij
Syr. tolu	℥j
Aq. chlorof.	ad ℥iij
One teaspoonful in water every two hours.	

Nolf especially favors the treatment with intravenous injections of arsenic, but emphasizes that the injections must be repeated a number of times, and that all that can be expected after the first few is a very slight improvement, in fact little more than that the patient ceases to get progressively worse. After many injections improvement occurs.

RESEMBLANCE OF SPIROCHETOSIS TO PULMONARY TUBERCULOSIS AND THE IMPORTANCE OF NON-TUBERCULOUS CAUSES OF HEMOPTYSIS. One cannot help being impressed, after reading of these cases of pulmonary spirochetosis, by the close resemblance which at least some of them bear to pulmonary tuberculosis. This is made even more marked by the prevalence of hemoptysis in these spirochetal infections. Undoubtedly

it is true that blood-spitting from the lungs is, in the majority of cases, due to pulmonary tuberculosis, and it is quite proper not only because of this numerical probability, but also because of the importance of keeping the possibility of tuberculosis always in mind that we should continue to think first and foremost of tuberculosis when we encounter an instance of hemoptysis. On the other hand, however, it is also true that there are a great variety of causes which more or less infrequently may bring about a hemoptysis and which are in no way related to tuberculosis. We should therefore, while always first thinking of tuberculosis, not be unwilling to consider the other possible etiological factors.

At the risk of its being thought too elementary I have introduced at this point a list which includes most of the causes of hemoptysis:²⁸⁰

A. Hemoptysis due to changes in the lungs.

1. Tuberculosis: (a) early; (b) later.
2. Cirrhosis of the lung: pneumoconiosis from various causes.
3. Cardiac disease, especially mitral stenosis.
4. Violent coughing efforts, as in whooping-cough or bronchitis.
5. Injury to the chest:
 - (a) Following trauma to the chest wall.
 - (b) Fractured rib.
 - (c) Exploratory needling.
 - (d) At the end of paracentesis thoracis.
6. Lobar pneumonia.
7. Bronchopneumonia.
8. Septic pneumonia, with or without abscess.
9. Gangrene of the lung.
10. Infarction of the lung: (a) embolic; (b) thrombotic.
11. Neoplasm of the lung, whether primary or secondary.
12. Sporotrichosis of the lung:
 - (a) Aspergillosis.
 - (b) Actinomycosis.
 - (c) Other forms.
13. Aortic aneurysm pressing on and opening into the lung, bronchus or trachea.
14. Empyema, especially when interlobar.
15. Hepatic abscess bursting into the lung.
16. Hydatid cyst.
17. Primary atheroma of the pulmonary arterioles.

B. Hemoptysis due to changes in the bronchioles, bronchi or trachea:

1. Bronchitis: (a) acute; (b) chronic; (c) plastic.
2. Bronchorrhea.
3. Bronchiectasis.
4. Ulceration of the trachea or a bronchus.
 - (a) Tertiary syphilitic.
 - (b) Malignant; primary or secondary.
 - (c) Secondary to a foreign body.
 - (d) Secondary to a caseous or calcareous bronchial gland.
5. Parasitic infection by *Distoma pulmonale westermanni*.

²⁸⁰ Somewhat modified from that given by French, Herbert: *An Index of Differential Diagnosis of Main Symptoms*, p. 286.

C. Hemoptysis due to changes in the larynx.

D. Hemoptysis due to changes in the blood.

1. Purpura.
2. Scurvy.
3. Leukemia: acute or chronic; lymphatic or splenomedullary.
4. Anemia: pernicious or severe secondary.
5. Malignant types of specific fevers such as variola or measles.
6. Hemophilia.

E. Doubtful causes of hemoptysis.

1. Chronic glomerulonephritis.
2. Arteriosclerosis.
3. Vicarious menstruation.
4. Recurrent hemoptysis in arthritic subjects.
5. Hemoptysis in apparently sound and healthy young subjects.

This extensive list is not quite complete and fails, as all such compilations must, to place emphasis where it is due. Some of the causes detailed are extremely rare and many others would not, by their very nature, enter into the question we are discussing. There is, however, a not small group of causes which might bring about a hemoptysis closely resembling one due to tuberculosis and under conditions which would simulate this latter disease.

Spirochetosis has been discussed sufficiently to make it clear that not only the symptoms including hemoptysis, but also the physical examination and course of the disease may closely simulate tuberculosis. The resemblance of pulmonary syphilis is well known. Streptothricosis or actinomycosis of the lungs may also resemble tuberculosis in symptoms and signs, or the two diseases may be present together. Bridge²⁸¹ has seen 15 cases of such pulmonary actinomycosis, in none of which was the lung lesion secondary to the disease in other parts of the body. One of his cases is described as follows: A middle-west farmer of forty came with a casual picture of rapid phthisis, but no tubercle bacilli were found—only swarms of actinomyces. He expectorated unbelievable quantities of fetid mucus and blood for many weeks continuously—sometimes a pint in twenty-four hours. The whole left lung was more or less involved, the upper part most. There was a little fever, moderate emaciation and the patient was up and about most of the time. Gradually the expectoration lessened and the man recovered after several months, with a large mass of consolidation in the upper third, reduced vesicular murmur and bronchial breathing over the whole left lung. He had continued well three years afterward.

Other forms of mycosis of the lungs also may simulate tuberculosis. Nathan²⁸² has recently emphasized this in connection with oidiomycosis. He states that oidiomycosis very closely resembles tuberculosis, and he suggests that certain cases not originally tuberculous are sent to a tuberculosis sanatorium under a mistaken diagnosis and there become infected with the second disease. Only by the discovery of the fungi in the sputum can the diagnosis be made, and this is of great importance,

²⁸¹ Contributions to Medical and Biological Research, 1919, i, 337.

²⁸² Bulletin of Medicine, July 3, 1920, xxxiv, 608.

as treatment with iodides is remarkably successful. Nathan reports the case of a young woman who had been treated at a sanatorium for two years under the belief that her condition was tuberculous. Complete cure followed two weeks of treatment with iodides. Le Blanc²⁸³ has reported 2 cases which had been diagnosticated as pulmonary tuberculosis and which he believes were due to sporotrichosis. The sporothrix of Schenk was discovered in a submucous granuloma in the throat.

Confusion of unresolved pneumonia with tuberculosis is not uncommon. Overend²⁸⁴ has recently emphasized the danger of this after pneumonia in children.

Before leaving this subject of non-tuberculous hemoptysis, mention must be made of two types of familial or hereditary hemoptysis. One is due to the well-known condition "familial multiple telangiectasis." This depends for the production of hemoptysis upon the rupture of minute telangiectases in the throat or nose or on the tongue or buccal mucous membranes. These telangiectases appear in a number of members of a family without exhibiting any special tendency to appear in one sex or the other; nor does sex seem to play a determining rôle in transmission. Nose-bleed is the usual symptom, but hemoptysis may also be complained of. In the family recently reported by Goldstein,²⁸⁵ some of whose members I had an opportunity to examine, there were 11 instances of this peculiar trouble, at least 2 of whom had died from the results of the repeated epistaxis. Osler was one of the first to establish the identity of this condition and not over forty families have been reported. Whether such telangiectases may occur in the bronchi or trachea alone is not known, but if this were so and the family history not in evidence, the resulting picture would be most confusing. Libman and Ottenberg²⁸⁶ have described a family in which this possibility was discussed but no telangiectasis could be found by bronchoscopy performed on two members of the family. Their article is entitled, "Hereditary Hemoptysis," and is a report of the study of a family in which seven members gave practically identical histories—numerous hemoptyses commencing in adult life and not interfering with the general health. There were no cases of tuberculosis in the entire family, although at least one had been suspected on account of the bloody spitting. None of the family were bleeders in any other sense; none bled inordinately from accidental wounds. The blood of the patient most thoroughly studied did not exhibit the characteristics of hemophilia or of chronic purpura; the coagulation time, bleeding time and platelet count were within normal limits. In no instance did the bleeding appear before the age of puberty, nor did it in any instance appear to shorten life. The most careful study failed to reveal any etiology.

Pleural Spirochetosis. One further aspect of infection of the respiratory tract with the spirochete of Castellani should be mentioned. It concerns the involvement of the pleura and the interest centers in a case recently reported by Mason.²⁸⁷ The patient was a boy, aged six-

²⁸³ Illinois Medical Journal, December, 1920, xxxviii, 516.

²⁸⁴ Tubercle, September, 1920, i, 547.

²⁸⁵ Archives of Internal Medicine, January, 1921, xxvii, 102.

²⁸⁶ Contributions to Medical and Biological Research, 1919, i, 632.

²⁸⁷ Johns Hopkins Hospital Bulletin, December, 1920, xxxi, 435.

teen years, who had always been healthy until in January, 1920, he developed an acute febrile illness which was believed to be influenza. From this illness he never completely recovered; the cough continued and a constant dull pain under the left shoulder-blade. The sputum was often very foul and once contained blood. About six months from the onset of his illness he suddenly became more sick, with a chill, high fever and severe pain in his left chest. He had marked breathlessness, severe cough, delirium and drenching sweats. On admission to the hospital, June 18, 1920, it was noted that the patient looked very ill, was cyanotic and dyspneic. There was fever of irregular type rising occasionally to over 102°. Cough was only occasional and was unproductive; the breath had a peculiar fetid odor. Physical examination revealed the typical signs of fluid and air in the left pleural cavity. Pinkish milky fluid was withdrawn through a needle. It had a peculiar fetid odor and upon fresh examination was found to contain large numbers of pus cells, a few erythrocytes, some cocci and bacilli and many actively mobile spirochetes. The presence of the spirochetes was confirmed by stained specimens and by dark field examination. No fusiform bacilli could be found and all cultures were negative. Open drainage was established and about 700 cc of pus removed, following which the patient was critically ill for several days. On the fifth day neosalvarsan was administered intravenously. Improvement from this time was rapid, but three further injections of neosalvarsan were given. The patient gained rapidly and at the date of publication was completely recovered except for slight discomfort caused by a partial left pneumothorax.

Mason's explanation of this case is that the illness of several months' duration which preceded the admission to the hospital was produced by an infection of the lungs with spirochetes, and that during an attack of coughing an area of pulmonary gangrene was ruptured and spirochetes were admitted into the pleural cavity. Pyopneumothorax resulted. According to Mason this is the only recorded instance of empyema with the presence of spirochetes in the pus. He refers to the report by Lancereaux²⁸⁸ of the finding of spirochetes in the bloody fluid from a hemothorax due to a penetrating war wound of the chest. In that instance it seems probable that the spirochetes were introduced by the missile causing the injury. In the case reported by Lancereaux there was a definite leukocytosis, but there was present a mixed infection. Mason does not record the blood picture. Mason gives a very full list of references on pulmonary spirochetosis which will be very helpful to anyone desiring to read the literature on this subject.

In Mason's case, as in all the others, the recognition of the condition has depended upon the discovery of the spirochete, and this emphasizes again the importance of the examination of the sputa of patients with respiratory disease for this group of organisms. This is especially stressed by Levy²⁸⁹ in reporting 2 cases occurring in Texas. Neither of his patients were febrile; one was a chronic case resembling tuberculosis and the other a more acute process suggesting influenza. It is inter-

²⁸⁸ Presse méd., October 1, 1919, xxxvii, 556.

²⁸⁹ New York Medical Journal, January 29, 1921, cxiii, 186.

esting to note that in this latter case there was no leukocytosis. In both cases the sputa contained spirochetes conforming to the Castellani type.

Treatment of Pulmonary Disease. OXYGEN INHALATIONS. Rudolf²⁹⁰ has recently reviewed the various views on this subject and comes to the following conclusions:

1. Oxygen is of value whenever a state of anoxemia exists. This is universally recognized in cases of mountain sickness and sickness from high flying, and in poisoning by CO, nitrites and arseniuretted hydrogen and also in the effects of enemy gas.

2. For the same reasons oxygen should be tried in all cases of cyanosis and also in acute respiratory conditions such as pneumonia when anoxemia threatens.

3. The ordinary method of giving oxygen by holding a funnel connected with the oxygen cylinder near the face of the patient is practically useless.

4. A better method than this is to give the gas through a rubber tube inserted into one nostril, and this may be made more effectual if the opposite nostril be rhythmically compressed during inspiration, the mouth, of course, being kept closed.

5. The oxygen chamber is a very effectual way of giving oxygen, especially in chronic cases, but it involves much expense and care.

6. An extremely useful and effectual appliance for the administration of oxygen is Meltzer's apparatus for oral insufflation.

Rudolf refers to a report by Meakins,²⁹¹ who, by giving oxygen with the Haldane apparatus, was able to increase the oxygen content of the blood of the cyanosed pneumonia patient to above that of the normal individual. No better evidence than this could be needed of the value of oxygen inhalation in "anoxemia."

REGULATION OF BLOOD CONCENTRATION is suggested by Underhill and Ringer²⁹² as a valuable method of treatment in influenza. In influenza as in acute phosgen gas-poisoning the blood becomes greatly concentrated, and this constitutes a factor of the greatest importance in the fatal outcome. The same treatment which was evolved for acute phosgen gas-poisoning has been applied with success in a few cases of influenza. The method consists in the maintenance, under carefully controlled conditions, of blood concentration as near the normal level as possible by venesection and fluid introduction. Blood concentration means a failing circulation, an inefficient oxygen carrier, oxygen starvation of the tissues, fall of temperature, and, finally, a suspension of vital activities. The changes in the concentration of the blood can best be followed by accurate hemoglobin estimations, and an attempt is made in those cases in which an increase of blood concentration develops to restore it to normal by bleeding and the introduction of fluid into the body by way either of the mouth or of the vein. The activity of treatment must be regulated by the changes in blood concentration; usually

²⁹⁰ American Journal of the Medical Sciences, 1920, clx, 10.

²⁹¹ British Medical Journal, 1920, i, 324.

²⁹² Journal of the American Medical Association, 1920, lxxv, 1531.

two or three bleedings of 250 cc each, supplemented with a sufficient intake of water, will inhibit blood concentration from attaining a dangerous height.

TREATMENT OF PULMONARY GANGRENE. The use of neoarsphenamin in the treatment of gangrene of the lung is claimed to be of great value by Reichmann,²⁹³ Stepp²⁹⁴ and others. The cases they report were of various kinds and in only one were spirilla found in the sputum. It seems improbable that all of the cases were actually instances of spirillosis, and yet it is equally probable that it is in this limited group that such treatment would be of greatest value. More careful study of cases is indicated and a conservative attitude adopted until it is found whether this treatment has any usefulness outside the spirillar cases. The subject of gangrene of the lung due to spirillosis and its treatment has been referred to earlier in this article.

Guisez²⁹⁵ has employed a 1 per cent solution of menthol, or a 5 per cent solution of guaiacol in an oil solution for intrabronchial injections in the treatment of gangrene of the lung. He claims considerable improvement.

DRUG-TREATMENT OF TUBERCULOSIS. Sodium morrhuate has been used by Biesenthal²⁹⁶ in 25 cases. As a result he cannot agree with the claims which have been advanced for it.

Sodium cinnamate has been studied experimentally by Corper, Gauss and Gekler.²⁹⁷ The results do not appear conclusive as yet.

Krysolgan (a sodium salt of P-amino-O-aurophenol carbonic acid which contains about 50 per cent of gold) has given useful results according to Geszti²⁹⁸ and Rickmann.²⁹⁹ It is supposed to bring about a focal reaction with subsequent repair. The focal reaction appears to be provoked by the deposit of gold in the diseased areas for which it is supposed to have a selective action.

Cerium salts are being carefully studied by a group of French investigators to determine, if possible, their usefulness in the treatment of tuberculosis. Grenet and Drouin³⁰⁰ have obtained some results which Renon³⁰¹ refers to as "the most scientific yet realized in the chemotherapy of tuberculosis." Their work has continued for over eight years, and one is made optimistic by the careful and conservative tone of their reports.

To date, however, no such treatment has stood the test of time and experience. All have gone to join von Linden's "copper lecithin" compound and the Japanese "cyanocuprol," in the group of preparations which apparently have not settled the tuberculosis problem. A most lucid editorial,³⁰² during the past year, pointed out some of the diffi-

²⁹³ *Therap. Halbmonatsh.*, 1920, xxxiv, 442.

²⁹⁴ *Ibid.*, p. 161.

²⁹⁵ *Presse méd.*, 1921, xxix, 162.

²⁹⁶ *American Review of Tuberculosis*, 1920, iv, 781.

²⁹⁷ *Ibid.*, 1920, iv, 464.

²⁹⁸ *Beitr. z. Klin. d. Tuberk.*, 1920, xliii, 235.

²⁹⁹ *Ztschr. f. Tuberk.*, 1920, xxxii, 16.

³⁰⁰ *Bull. d. l. Soc. Méd. d. hôp. de Paris*, 1920, xlv, 589.

³⁰¹ *Ibid.*, p. 606.

³⁰² *Journal of the American Medical Association*, 1920, lxxv, 246.

culties which surround this problem of the chemotherapy of tuberculosis. Before accepting new and unproved treatments it would be well for us to read that editorial, and ask ourselves if those who are advancing some new "synthetic" are capable and in a position to have properly determined its curative value.

Diseases of the Pleura. Syphilitic pleurisy has been repeatedly described, and Schupfer³⁰³ has recently reported a case which would apparently fall in this class. He, however, believes that this case, as well as the vast majority of similar cases, are truly of tuberculosis etiology. That such a tuberculous pleurisy should develop in a syphilitic individual is not surprising, nor must one assume too certain a relationship between such a pleurisy and the syphilis merely on the basis of a positive serological test and on the beneficial influence of antileptic treatment on the pleurisy. Many cases of pleurisy thought to be of syphilitic nature have later developed undoubted tuberculosis.

PLEURAL EFFUSION WITH ACUTE BRONCHITIS is not usually expected, but Petzétakis³⁰⁴ claims to have demonstrated a small collection in three-quarters of 54 cases of simple acute bronchitis which he studied. The amount of the effusion is very slight, usually less than 20 cc, and it is often not demonstrable by roentgenograms.

SUBCUTANEOUS EDEMA WITH PLEURISY is described by Lussana and Arrigoni³⁰⁵ in what they consider a unique case. The pleurisy was bilateral and of a simple acute serofibrinous type. The edema resembled edema from stasis and involved the subcutaneous tissues from the scapula to the sacrum. The report is unconvincing.

DANGERS OF PUNCTURE OF THE PLEURA are touched on by Apert and Vallery-Radot³⁰⁶ in connection with the sudden death of a four-year-old boy following exploratory puncture. The explanation in this case, however, was undoubtedly a diphtheritic myocarditis which was recognized at necropsy. The part played by a diseased heart in such catastrophes is no small one, and great care and watchfulness should be exercised in performing thoracic puncture in cases with disease of the heart, especially of the myocardium. That the danger depends chiefly on alterations in intrapleural pressure brought about by the aspiration rather than on the simple puncture is the opinion expressed by Flurin and Rousseau.³⁰⁷

CONCERNING PLEURAL EFFUSION. Graham³⁰⁸ has attempted experimentally to study the influence of the respiratory movements on the production of pleural effusions. He constructed a model thoracic cavity into which lungs could be introduced. The lungs were automatically inflated and deflated to simulate the respiratory movement. When edematous lungs were used in the model a copious "pleural exudate" could be produced, but, contrary to expectation, most of the fluid came out at the end of inspiration. The experiments are admittedly crude,

³⁰³ *Riforma med.*, 1921, xxxvii, 25.

³⁰⁴ *Lyon méd.*, 1920, cxxix, 696.

³⁰⁵ *Políclinico*, 1921, xxviii, 217.

³⁰⁶ *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1920, xlv, 852.

³⁰⁷ *Ann. de Méd.*, 1920, vii, 325.

³⁰⁸ *Journal of the American Medical Association*, 1921, lxxvi, 784.

but they are important and help to explain the rapid formation of pleural exudates, as for example during a streptococcal bronchopneumonia.

The removal of particulate matter from the pleura has been studied by Karsner and Swanbeck.³⁰⁹ Carmine and lamp-black were the substances employed, and the material was injected into the pleural cavities of cats. It was found that particles were taken up by the endothelial cells *in situ* and transported by the cells rather than as free pigment. The cells of the parietal pleura were perhaps more actively phagocytic than those of the visceral pleura. Drainage from the parietal pleura is chiefly into mediastinal lymph nodes, whereas that from the visceral pleura is principally into the lymph nodes at the hilus of the lung. One very interesting observation was the occasional transfer of the pigment to the abdominal lymphatic apparatus. This may have a bearing on some of the obscure abdominal symptoms and complications seen with thoracic disease, for bacteria might be transferred as well as pigment granules.

PRIMARY NEOPLASM OF THE PLEURA is discussed by Du Bray and Rosson.³¹⁰ Their summary is as follows:

1. Primary, malignant and pleural tumor is a very rare condition.
2. These tumors constitute a distinct group and present a rather constant pathological picture.
3. The definite point of origin of these neoplasms has not been determined absolutely.
4. We favor the mesothelial origin and prefer to designate the tumor as mesothelioma rather than carcinoma, notwithstanding the fact that most of these neoplasms have been reported under the term endothelioma.
5. In this case the clinical diagnosis of malignant pleural disease was substantiated by the necropsy findings.
6. Pain in the chest is the earliest and most significant single symptom. It is usually severe and persistent in character and presents the most distressing feature of the disease.
7. The clinical course is of comparatively short duration and is usually afebrile.
8. There is nothing pathognomonic in the physical signs of the disease. A persistent, rapidly reaccumulating, hemorrhagic, pleural fluid is suggestive, and in its presence the possibility of pleural new growth should always be kept in mind.
9. The clinical picture studied as a whole offers the most valuable and trustworthy evidence.
10. The roentgen-ray examination fails to determine the exact nature and site of origin of the disease process in pleural malignancy.
11. Cytodiagnosis and the chemical study of the pleural transudates are of very limited value.
12. In those instances in which an exhaustive study has failed to establish a diagnosis, and pleural malignant disease is suspected, an exploratory thoracotomy is justifiable.

³⁰⁹ Journal of Medical Research, 1920, xlii, 91.

³¹⁰ Archives of Internal Medicine, 1920, xxvi, 715.

13. The two most important and at the same time difficult diseases to exclude in the differential diagnosis are pulmonary tuberculosis with hemorrhagic pleural effusion and primary malignant disease of the lung or bronchus.

PNEUMOTHORAX. Little new has been reported on this subject. Stivelman and Rosenblatt³¹¹ call attention to the occurrence of multiple fluid collections in the chest in the course of pneumothorax induced for therapeutic purposes. The fluid, they claim, collects above pleuritic adhesions which spread out in hammock-like fashion from one pleural layer to the other. The condition can only be recognized with the roentgenograph; in 32 cases of hydropneumothorax so studied the presence of multiple fluid collections could be demonstrated in 5 cases.

Hale³¹² reports a case in which it is claimed there was a hernia of pleura near the scapula. The patient had a spontaneous tuberculous pneumothorax which communicated with the pleural hernial sac. No autopsy confirmation is reported.

A short review of the subject of spontaneous pneumothorax was published by Gray.³¹³ He emphasizes that dyspnea should never be regarded as an ordinary concomitant of pulmonary tuberculosis. Its advent should always be considered as an urgent indication for a complete survey of the chest. Spontaneous pneumothorax is far more common than is usually supposed.

EMPHYEMA. The literature on this subject continues to be extensive, but for the most part it is concerned with the treatment, and little attention is paid to the etiology, which is obviously the most important aspect. Prevention, or at least the early non-surgical treatment, is what must be hoped for. Concerning the etiology it is interesting to note that Moschcowitz,³¹⁴ in his article on the pathogenesis and treatment of empyema, makes the statement that "empyema in most instances results from the rupture of a small subpleural pulmonary abscess." He also says: "An empyema is the final stage of a process in which the first stage is a serous pleurisy and the second a seropurulent pleurisy." It is a little difficult to correlate these two conclusions, and one is tempted to suspect that the rupture of a small pulmonary abscess is a relatively rare cause of empyema.

Bacteriological studies of a series of cases of empyema were made by Gordon,³¹⁵ who reports that the pneumococcus and streptococcus were found to be the principal primary invaders, while a variety of other bacteria may be introduced at the time of operation. Staphylococcus albus and aureus and diphtheroids and chromogenic air bacteria were among the frequent secondary infecting agents.

Vidfelt³¹⁶ found the streptococcus responsible for 70 of his 127 cases of empyema following influenza. This finding agrees with many others,

³¹¹ American Journal of the Medical Sciences, 1921, clxi, 229.

³¹² Medical Record, 1921, xcix, 16.

³¹³ Journal of the American Medical Association, 1921, lxxvi, 1147.

³¹⁴ American Journal of the Medical Sciences, 1920, clxi, 669.

³¹⁵ Journal of Infectious Diseases, 1920, xxvi, 29.

³¹⁶ Hygeia, 1920, lxxxii, 545 (abstract, Journal of the American Medical Association).

and so does his conclusion that a preliminary thoracentesis in the streptococcus cases with secondary thoracotomy gives much better results than primary thoracotomy.

Renaud³¹⁷ advises neglecting the pleural complication until the acute pulmonary process is over. Treatment should be directed at supporting the heart and circulation. He believes the plural collection is of relatively little importance in comparison with the infection.

Treatment of Empyema when once it is established must still be by operation. As yet no satisfactory antiseptic fluid for injection has been discovered, although the search is still being continued. Ashhurst³¹⁸ believes that the injection of antiseptic fluids into the unopened pleura is usually detrimental to the patient. He lays emphasis on the importance of searching for concealed collections of pus and of supplying adequate drainage for these areas when localized. His method of exploratory thoracotomy is peculiarly valuable for this purpose.

Probably the most important work relating to the treatment of empyema is that by Graham.³¹⁹ His experiments and human observations prove conclusively that one can approximately estimate, from determinations of the vital capacity of the lungs, how large an opening in the chest wall will be compatible with life. This principle applies only to cases in which the mediastinum is not already stabilized by adhesions and induration. For example, an individual who has an average vital capacity of 3700 cc and a normal thorax can live with an opening in the chest wall of 51 square cm. or 8 square inches. This work is of special interest to the surgeon and will probably be found more fully reviewed elsewhere, but to the medical man it presents several points of importance. It is an additional and a strong argument against the establishment of an open drainage during the acute pneumonia stage of an empyema when the vital capacity is markedly low as compared with the air requirements of the body. After the mediastinum is fixed there is less effect of an opening on one side upon the opposite lung. But it is even claimed that in a normal chest a bilateral open pneumothorax is practically no more dangerous to life than a unilateral opening, provided that in each case the areas of the openings are within the determined limit.

Diseases of the Mediastinum. **NEOPLASM.** Mention should be made of a case reported by Leopold.³²⁰ The patient, a man, aged thirty-seven years, was well until about a year and half before his death. He first developed a deep, hollow cough which became more persistent and was of an irritating character. In about four months this amounted to shortness of breath and an occasional wheezing. During the next five months the cough and dyspnea grew rapidly worse and it became necessary to sit upright or to lean forward. By this time he had lost about ten pounds in weight. Roentgen-ray treatment seemed to give

³¹⁷ Bull. d. l. Soc. méd. d. hôp. de Paris, 1920, xlv, 1334.

³¹⁸ Annals of Surgery, 1920, lxxii, 12.

³¹⁹ Surgery, Gynecology and Obstetrics, 1920, xxxi, 60; Journal of the American Medical Association, 1920, lxxv, 992.

³²⁰ Archives of Internal Medicine, 1920, xxvi, 274.

a temporary relief, but he continued to grow weaker and thinner. By the fifteenth month the air hunger was continuous; the edema of the lower extremities, genitalia and abdomen was extreme. Marked cyanosis of the upper extremities, and especially the head, appeared; later numbness of the arms, mental torpor and finally death. The record of the physical signs is not obtainable, but a roentgenogram taken nine months after symptoms developed resulted in a diagnosis of large primary tumor in the anterior mediastinum. On opening the thoracic cavity at necropsy the entire cavity appeared to be filled with an indefinite, lobulated mass conforming to the thoracic arch and extending from the apex to the diaphragm. The mass seemed to be attached only at one point, just below the sternal notch, and by only a frail strand of loose "adhesive-like" bands, easily dissected free with the fingers. The base and posterior surface were found free and the entire mass was easily delivered, disclosing the heart, vessels and lungs compressed along the vertebral column and low in the posterior mediastinum. The tumor mass was soft and fluctuating and covered by a fibrous capsule. On cross-section it was apparently a mass of pale yellowish, greasy, fatty tissue. The mass weighed 17 pounds 6 ounces and measured 31 x 30 x 15 cm. (12 x 12 x 6 inches). Microscopically the tumor was found to be composed entirely of masses of fat cells lying in a vascular connective-tissue matrix.

Leopold found in the medical literature more references to other primary tumors of the mediastinum than to primary lipoma. Teratoma, dermoid cysts, fibroma and other tumors appear occasionally, but he could find only four cases of lipoma reported. This case is apparently unique in the size of the lipoma in this region.

Foot³²¹ reports the finding of a malignant thymoma in the mediastinum of a boy, aged nine years, who died during anesthesia for an exploratory operation. It lay chiefly in the anterior mediastinum, directly under the sternum, but not infiltrating the bone. There was some local extension to the surface of the lungs and elsewhere.

Lorenzini³²² describes a case of lymphosarcoma of the mediastinum in a girl, aged six years. Repeated removal of fluid from the pleural cavity was necessary, 8000 cc being obtained by nine punctures. The picture at first was that of a left-sided pleurisy with effusion, but soon the left arm showed edema and the displacement of the heart toward the right was not modified by the removal of the effusion. Death occurred in a few weeks from asphyxia.

Lewis³²³ reports the apparent disappearance of a mediastinal neoplasm as a result of treatment with the roentgen ray and radium.

³²¹ American Journal of Diseases of Children, 1920, xx, 1.

³²² Riv. di clin. pédiat., 1920, xviii, 129 (abstract, Journal of the American Medical Association).

³²³ Lancet, 1920, ii, 1092.

DERMATOLOGY AND SYPHILIS.

By JAY F. SCHAMBERG, M.D.

Eczema. Hazen¹ reports the results of a study of 195 patients with eczema conducted for the purpose of determining the etiology.

An idea of the variable causes of this disease will be obtained from the following method of study pursued by Hazen. An effort was made to find external irritating factors. Inquiries were made as to the use of soap and water, the effect of the use of a scrub-brush or of sand for cleansing purposes; the effect of cold and windy weather or of hot weather and excessive perspiration; the wearing of wool or fur next to the skin or the use of blankets at night; the use either accidentally or intentionally of various chemical substances such as hair tonics, face creams or of various irritating substances used in the arts, trades or professions; the care of flowers, especially of the primrose and many similar greens.

The following table shows the results:

CAUSE OF ECZEMA IN PATIENTS EXAMINED.		Cases.
Local irritation:		
Soap and water		36
Weather		6
Occupation or chemicals		30
Clothing		18
Plants		6
Total		96
Local infection:		
Bacterial		4
Epidermophyton		2
Total		6
Local predisposing causes:		
Excessive sweating		16
Frostbite		1
Varicosities		5
Xeroderma		3
Total		25
Internal causes:		
Disturbed vegetative nervous system		14
Disturbed food assimilation, eczema of children		12
Urticaria		7
Total		33
Combined causes		9
Undetermined causes		26

¹ Archives of Dermatology and Syphilis, June, 1920.

A search for epidermophyton fungus was made in all suspicious-looking lesions on the hands, feet and crural region.

In some instances in which bacterial infection was suspected, a bacterial study was made and auto-inoculation experiments carried out on the patient.

All doubtful cases were studied by an internist. All children were studied by a pediatrician. Roentgenograms were taken of the teeth in many cases, and in some instances teeth showing root abscesses were extracted. In cases in which there was a history of intestinal trouble, roentgen-ray studies were made of the digestive organs. Cutaneous food tests were applied to all doubtful cases.

Hazen particularly discusses the cases of eczema associated with disturbances of the vegetative nervous system, and clinically usually showing signs of a vagotonia. The common symptoms of vagotonia are: Slow heart action, often irregular; bronchial asthma, acute attacks of rhinitis with a profuse discharge lasting a short time; pyloric stenosis; spasm of the colon and sudden attacks of urticaria or of an acute dermatitis resembling eczema. The sympatheticotonic shows an opposite set of symptoms.

In dermatitis associated with disturbances of the vegetative nervous system, the lesions usually begin on the flexures of the elbows and knees, and frequently on the sides of the neck, radiating from the sternoclavicular articulation up under the ear. Larger surfaces may be involved secondarily. The axillæ or groins may be invaded at the time of the initial attack, but this is rather unusual. The lesions may be erythematous, but are more frequently distinctly papular; they may also become vesicular, and if there is much itching, as there often is, there may be considerable weeping as the result of the irritation produced by scratching. These lesions are spoken of under a large variety of names, such as neurodermatitis and other names collected by Wise.

Disturbances of the vegetative nervous system may be due to, (1) a protein hypersusceptibility, either to a food or to bacteria (focal infection); (2) possibly to mechanical irritation, such as teething; and (3) to psychic irritation.

Hazen summarizes his views concerning the etiology of eczema as follows: Eczema, while giving a definite clinical picture, is in reality due to the following causes: External irritation, external infection, local predisposition of the tissues, disturbances of the vegetative nervous system, disturbed food assimilation and urticaria, the latter probably being due to a protein hypersusceptibility.

The day will come when the word "eczema" will no longer be used, just as the word "rheumatism" is now passing from usage. There is no more relationship between a dermatitis due to external irritation and one due to vagotonia than there is between a gonorrheal arthritis and a syphilitic one.

As clinical entities now well established the following may be suggested. Dermatitis due to external irritation; vagotonic dermatitis; urticarial dermatitis and dermatitis due to disturbed food assimilation (the eczema of young children). None of these conditions should be classified

as eczema, as this only results in confusion and a failure to discover the cause.

The term eczema should be limited to an inflammation of the skin arising from internal cause, whereas the term dermatitis should be limited to an inflammation of the skin due to a variety of irritating substances coming in contact with the skin. These terms have only an etiological distinction, since the cutaneous inflammations due either to an external or internal cause do not differ pathologically, and in many instances it is not possible to differentiate it by clinical features.

This distinction between eczema and dermatitis is, nevertheless, desirable, since it tends to clarify, at least etilogically, the conglomerate conception of what we know clinically as eczema. However, the term eczema and dermatitis are frequently used interchangeably.

It is apparent from the above considerations that there is no essential cause for eczema and that the same pathological phenomenon is due to a variety of causes.

Hence one may speak of internal and external causes of eczema. The external causes embrace a large number of chemical substances, drugs, dyestuffs, plants and indeed mechanical irritation, such as scratching, rubbing of clothes, etc. The internal causes are less tangible in nature, but are, doubtless, substances the result of disordered metabolism of gastro-intestinal, hepatic and renal origin.

In short, then, any irritant of internal or external origin may, in a susceptible skin, produce eczema—the susceptibility is represented in an abnormal irritability of the skin; the basis, however, of this susceptibility is not understood. This phase of the etiology of eczema is discussed by Harris.² He expresses the belief that the important factor in the production of an eczema is an increased irritability of the skin or of some structure in it, this abnormal irritability resulting in a reaction of the skin to irritants of varying degrees of intensity. Thus a skin in this state of unstable equilibrium would react to an irritant of any type, be it ever so mild. A skin in a state of normal equilibrium would require an irritant of great intensity, the reaction in this case being called an artificial dermatitis. A skin in a highly irritable state could react to a stimulant so mild as to be considered physiological. Many facts, clinical and experimental, Harris thought, substantiate this view of the etiology of eczema. It is conceded that eczema is an inflammatory reaction of the skin. The normal skin of eczema patients is especially sensitive to external irritation, be it mechanical, chemical or thermal. The sensation of itching is inherent in the epidermis, is a prominent symptom of eczema and can be prevented and counteracted by adrenalin. Inflammation of the conjunctiva and skin, usually resulting from the use of strong irritants, can be prevented by paralyzing the reflex arc in various ways, among which is the local or subcutaneous use of adrenalin. Since the vasomotor changes in eczema are so intimately associated with itching, and it has been shown that adrenalin prevents them both and is a normal constituent of the blood, it requires no great

² Archives of Dermatology and Syphilis, May, 1921.

imagination to suppose that a deficiency of the active adrenalin in the blood could account for the increased sensitiveness of the skin on the one hand and the itching on the other. The adrenalin might act on the cutaneous reflex arc. The rather frequent association of eczema, low blood-pressure and asthma, all conditions counteracted by adrenalin, in Harris's opinion, is suggestive, to say the least. On the other hand, some toxic substance, or substances which, entering the blood from time to time, might, in spite of a normal adrenalin content, act as an irritant to the vasomotor system, and especially to the cutaneous reflex arc or neutralize the normal adrenalin action at this point. The rather intimate association between eczema on the one hand and various metabolic and nervous disturbances on the other hand suggested such a possibility. The influence of diet and the gastro-intestinal tract, the action and formation of histamin, indican and antitrypsin as possible factors in the causation of eczema were also considered by Harris.

PROTEIN SENSITIZATION IN ECZEMA. A number of papers have recently appeared on protein sensitization in eczema. A series of 78 cases of eczema tested with various proteins by Ramirez³ gave positive skin tests in 30. Of the 30 positive cases, 14 were under the age of twenty years and 12 between twenty and thirty years of age. Of the thirty positive cases, 14 had an associated asthma and 2 an associated hay fever. Ramirez expresses the opinion that only a comparatively small percentage of eczemas are anaphylactic, but that the ones associated with asthma or hay fever are generally of this type.

Twenty-seven of the 30 positive cases reacted to more than one protein. The foods that gave positive reactions in the order of frequency are shown in the following table:

POSITIVE REACTION TO VARIOUS PROTEINS.		Cases.
Milk (cows')		4
Egg-white		14
Whole wheat		2
Corn		7
Rice		4
Rye		2
Oats		3
Pork		3
Potato		4
Lettuce		3
Celery		8
Cabbage		2
Herring		1
Lobster		1
Crabs		1
Veal		2
Beef		3
Ragweed		4
Timothy		2
Total		70

The skin scarification method was used and the reactions were called positive only when a definite wheal measuring 0.05 cm. in diameter

³ Archives of Dermatology and Syphilis, September, 1920.

appeared. The treatment of these patients consisted solely in the removal from the diet of the protein giving a positive reaction. In the cured and improved patients the improvement was noticed within the first week. In the apparently cured individuals there had been no recurrence with skin for months, and in some cases one year, although they were taking small quantities daily of the food to which they were originally sensitive. Skin tests performed six months later in 6 of the cured patients gave negative results. One of Ramirez's most striking results occurred in a woman, aged twenty-eight years, who had suffered for a year from an eczema of the hands. She reacted positive to banana and positive to celery. She had previously eaten bananas every morning for breakfast. After she omitted this food from her diet the eczema cleared up at the end of a week to return again in two weeks when she again ate bananas. She then stopped eating bananas and again the eruption disappeared and had not returned at the end of one year.

Fox and Fisher⁴ studied 60 cases of eczema for protein sensitization. These cases included various types of subacute and chronic eczema. Care was taken to exclude cases due to some known local irritant and those that might have had a parasitic or otherwise infectious origin. In testing for protein sensitization the skin scarification method was used.

Of the 60 patients tested, 41 gave entirely negative reactions, the number of proteins used in each case varying from 13 to 37 (an average of 24). The attempt was always made to test the foods that were ordinarily eaten by each individual patient. There were 19 patients that reacted positively to 1 or more proteins. Each individual was tested with 15 to 44 proteins (an average of 25). Five patients reacted to celery, 5 to cheese, 4 to bean and turnip, 3 to cabbage, lettuce and sweet potato; 2 to carrot, cauliflower, oat and potato, and 1 each to asparagus, beet, coffee, corn, grapefruit, onion, orange, oyster, plum, pork, rye, tomato and wheat. They considered a + reaction to be a wheal 0.5 cm. in diameter; a ++, 1 cm.; +++, 1.5 cm., etc. No account was taken of the accompanying erythema.

On this basis they observed in 1 patient five reactions of ++++ intensity (wheal of 2 cm.), namely, to bean, carrot, celery, lettuce and turnip. One patient gave a +++ reaction to oyster and in 8 patients ++ reactions were given to cabbage, carrot, cauliflower, celery, lettuce, sweet potato and turnip. The remainder of the foods mentioned above caused a + reaction. They were impressed by the fact that the great majority of reactions, and especially all of the severe ones (except that to oyster), were given by vegetables. They are of the opinion that the protein skin tests in eczema of adults is of therapeutic assistance only in a small proportion of cases.

Higman and Michael⁵ studied *protein sensitization in urticaria and allied conditions*, notably angioneurotic edema. In this paper appears a discussion of the various theories and an extensive review of the literature.

Cutaneous tests were made in 14 chronic cases of urticaria, in which

⁴ Journal of the American Medical Association, October 2, 1920.

⁵ Archives of Dermatology and Syphilis, November, 1920.

were obtained a total of 63 positive reactions: 37 were to vegetable and 26 to animal proteins. Eleven of the 12 cases reacted to more than one protein. Ten cases reacted both to vegetable and animal proteins.

The opinion is expressed that urticaria and angioneurotic are anaphylactic manifestations. They believe that the protein food tests are of great value, inasmuch as the tests indicate sensitization to a definite protein which, in treatment, is to be removed from the diet.

SKIN REACTIONS TO DRUGS. In 2 cases of idiosyncrasy to drugs, Mook⁶ applied the well-known cutaneous tests. One case was susceptible to apothesine, a local anesthetic, and the other to quinine, taken internally. The first patient was a dentist who had a subacute dermatitis of the fingers. The patient was informed that his eczema was due to some chemical that he was using in his work. Inquiry developed the fact that he was using apothesine as a local anesthetic. When preparing this solution he would invariably spill a few drops on his fingers.

Mook prepared a 1 per cent solution of apothesine and applied it to a small scarification on his forearm with water controls such as are applied in food sensitization tests. Within twelve hours a distinctly positive result was observed. As novocaine is said to be a drug similar to apothesine the experiment was repeated after recovery from the apothesine, with a similar result.

Another patient who was susceptible to quinine was tested by Mook in a similar way. At the site of inoculation there was a considerable reaction which lasted for more than twenty-four hours.

DERMATITIS DUE TO CONTACT WITH A GUINEA-PIG. Markley⁷ reports a unique case of dermatitis due to contact with a guinea-pig. The patient complained of recurring attacks of an erythematous and papular eruption involving the face, neck and chest and parts of the forearm. The eruption persisted for almost one year. During her stay in the hospital it entirely disappeared, but recurred when at home. It was discovered that the skin became immediately worse after cleaning the pen of a guinea-pig and allowing the animal to run over her shoulders. Disposal of the animal was followed by prompt and permanent disappearance of the eruption.

Experiments were carried out in which it was demonstrated that a piece of guinea-pig fur applied to the skin of the patient promptly resulted in a dermatitis. Singularly only the sensitized skin—that is, the skin which had developed the dermatitis previously—was sensitive to contact with this guinea-pig fur. Other kinds of fur exposed to the skin produced no reaction.

In reviewing the literature on protein sensitization in eczema, one is impressed by the variance of opinion and the results obtained. The latter can doubtless be explained by the differences in the technic employed—the scarification method or by intradermal injections, and the standards employed in reading positive reactions.

The scarification method consists of a small number of cuts, each about one-eighth inch long, on the flexor surfaces of the forearm. These

⁶ Archives of Dermatology and Syphilis, June, 1920.

⁷ Ibid., December, 1920.

cuts are made with a sharp scalpel, but are not deep enough to draw blood, although they do penetrate the skin. On each cut is placed a protein, and to it is added a drop of tenth-normal sodium hydroxide solution to dissolve the protein and to permit of its rapid absorption. At the end of a half hour the proteins are washed off and the reactions are noted, always comparing the inoculated cuts with normal controls on which no protein was placed. A positive reaction, consisting of a raised, white elevation or urticarial wheal surrounding the cut, appears in the majority of cases within fifteen minutes. The minimum positive reaction should measure 0.5 cm. in diameter.

The intradermal method consists of an intracutaneous injection of an aqueous extract of the protein to be tested. A positive reaction consists of a node which appears about twenty-four hours after the intracutaneous injection, and may persist for several days.

The scarification method is the one most commonly employed. This method appears to be more specific, since it separates closely related proteins and is not too sensitive. The intradermal method is probably less specific, as it does not separate closely related proteins. In many instances it is too sensitive. Moreover, this method is not as practicable for its application as the scarification method.

The proteins employed are the commercial preparations prepared by pharmaceutical houses; these appear to be satisfactory. The total number is about 85 and includes as well those of epidermal origin.

Space does not permit the discussion of the underlying principles of anaphylaxis as applied to cutaneous sensitization.

The relation of anaphylaxis and the relation of cutaneous sensitization to anaphylaxis are not clearly understood. Indeed, the relation of cutaneous tests to these phenomena is not definitely understood.

At times inconsistent positive cutaneous tests are obtained. A positive reaction with a certain protein may be obtained at one time and a negative reaction with the same protein at a different time. The offending protein does not in all cases give a positive reaction; on the other hand, proteins which are apparently not the offending ones may give a positive reaction. It therefore appears that hypersensitiveness of the skin is not necessarily associated with systemic hypersensitiveness, and therefore the findings in cutaneous tests should not be interpreted too specifically in regard to the body at large.

The cutaneous sensitization tests have not proved of as great a value as was formerly hoped. In my experience, only in a few instances have they given valuable information. In the majority of instances, however, they have proved great disappointments. I believe their principal application is in urticaria and in cases of eczema associated with asthma or hay fever, since in these cases the largest percentage of positive reactions with the offending protein is obtained. I have not found them to be of any great assistance in determining the etiology of eczema in infants and children and of least value in the eczema of adults.

In determining the cause of a dermatitis, an inflammation of the skin of external origin, as contrasted to eczema, which is of internal origin, the cutaneous tests are of greater practical utility. Their value in this

regard is demonstrated in the report of Mook, reviewed in this paper, in which the dermatitis was due to apothesine, and in the report of Markley, in which the dermatitis was due to contact with guinea-pigs.

In the cases in which it is possible to clinically differentiate a dermatitis from an eczema, one should, from a careful analysis of the history, endeavor to elicit the suspicious substance causing the dermatitis and by a cutaneous test with these substances the cause of the dermatitis may be established. The use of the cutaneous tests in the above instances is more satisfactory than their use in eczema, because we are virtually reproducing the disease, which leaves little doubt as to cause and effect; whereas in eczema the relation between the proteins giving a positive reaction and the cause of the eczema is not always a definite one.

Alopecia Areata. Sabouraud⁸ discusses the etiology of alopecia areata after a consideration of the possible causes. He comes to the conclusion there is not a single one that can withstand the investigation of our present-day knowledge. Alopecia areata appears as a syndrome in a number of conditions. It may be observed as a hereditary manifestation in some families. It occurs in connection with vitiligo or with exophthalmic goiter. It also occurs in women as a manifestation of a precocious or late menopause, or in the adult in connection with late eruption of the wisdom teeth. In a very few cases it has some connection with acquired or hereditary syphilis, especially in syphilis of the late type. This can be proved by the marked improvement which results from antisiphilitic treatment.

Sabouraud⁹ emphasizes the importance of the proper method of treatment of alopecia areata, and especially its necessity as a means of warding off the appearance of new lesions. One of the most common errors is the limitation of treatment to the one or more bald spots present when it is instituted. He gives as the first indication for treatment the prevention of the formation of new patches, and as the second indication the treatment of the patches themselves.

The therapy differs somewhat, depending on whether the disease is benign or grave, as evidenced by the rapidity of spreading, number of broken hairs, etc.

In the benign case the author prescribes for the entire scalp eau de Cologne, 300 cc, crystalline acetic acid, 10 gm., commercial formol, 1 gm. The following mixture is at the same time to be applied to the bald spots: Hoffmann's solution, 30 gm., and crystalline acetic acid, 1 gm.

Should a single new spot appear, it is necessary to institute a more rigorous form of treatment. For this purpose the following salve is to be applied daily to the entire scalp: Deodorized oil of cade, 10 gm.; vasolanolin, 20 gm.; yellow basic sulphate of mercury, 1 gm.; verbena oil, for fragrance, q. s.

To cause the regrowth of the hair on the bald spots the author believes that the following preparation is the most efficacious: Chrysophanic

⁸ Ann. de dermat. et de syph., April, 1920.

⁹ Presse méd., December, 1920.

acid, 30 cgm.; anesthesia chloroform, 30 gm. The tar mixture should be used at the same time on the rest of the scalp.

In alopecia of the beard, treatment is not successful. Because of the difficulties in using on the face the preparations given above the author recommends the following, the effect of which is problematic: Purified xylol and Hoffmann's solution in equal parts.

The article is concluded with emphasis on the importance of syphilis as one of the etiological factors in the cause of the disease.

Barber¹⁰ states that, in his opinion, alopecia areata is due usually, if not invariably, to focal infection. He has collected evidence to show that the *Streptococcus longus* is the usual infecting organism, but it is quite possible that others may sometimes be responsible. He indicates that alopecia areata may be a chronic anaphylactic phenomenon, the antigen being bacterial protein, absorbed from the teeth, tonsils, nasopharynx, etc.

In treatment the most important thing is to remove, as far as possible, every source of infection. Vaccines are used in addition. For the anemic iron and arsenic are given and dilute hydrochloric acid when hypochlorhydria exists, and other methods of internal medication are mentioned. Pure phenol or lysol is suggested locally as the best agent to improve the cutaneous blood supply.

Fox¹¹ reports the results obtained in the treatment of 50 cases of alopecia areata with *quartz lamps* (Kromayer and Alpine). The patients were treated, as a rule, at intervals of about one week. It was aimed to produce an erythema that would remain for at least one week. At times the erythema was accomplished by vesicles or bullæ.

He concludes that the quartz lamps (Kromayer and Alpine) are cleanly and convenient agents for the treatment of alopecia areata. The results in the series of 50 cases, though not brilliant, were at least satisfactory. More than half of the patients were followed to complete recovery, while in 78 per cent of the cases the new hair had at least begun to grow. The results were gratifying because he had never previously succeeded in following any considerable number of cases when using other methods of treatment. The patients would become discouraged too quickly and continue the usual habit of such cases of frequently changing both remedy and physician.

The cause of alopecia areata is as yet undetermined. The French school of dermatology has long regarded syphilis as an occasional auxiliary cause of the disorder. One most tenable theory concerning its causation is that it is a trophoneurosis. In support of this theory is clinical observation of its occurrence after mental stress and strain; its occurrence in those areas whose nerve supply has been injured by accident or in surgical operations; its experimental production by the excision of the second cervical ganglion.

Although in the majority of cases of alopecia areata the hair will eventually return spontaneously, its return can be hastened by treatment, stimulation by means of local application or by means of actinotherapy.

¹⁰ British Journal of Dermatology and Syphilis, January, 1921.

¹¹ Medical Record, November, 1920.

Of the numerous stimulatory ointments and lotions that have been proposed as treatment, I have found chrysarobin to be one of the most effective remedies when used in an ointment containing from 10 to 60 grains to the ounce: As for actinotherapy, I have found the Kromayer lamp a valuable aid in the treatment of alopecia areata.

It is difficult to arrive at definite conclusions as to the value of any one form of treatment of alopecia areata on account of the capricious nature of this malady. The hair may return spontaneously in a few weeks or it may not return for one or more years. The last remedy used is likely to be given credit for effecting the cure.

Acne Rosacea. A number of cases of acne rosacea were examined by Ryle and Barber,¹² with a view to determine, if possible, the actual pathogenesis of the condition and the most satisfactory method of treatment. The connection between this disease and dyspepsia is generally recognized, and it is usually supposed that overindulgence in alcohol, tea or coffee produces its effect by setting up a chronic gastritis. Twelve cases of acne rosacea were investigated by the fractional method of gastric analysis. In 5 there was complete achlorhydria throughout the period of the meal. In 2 cases there was an extreme degree of hypochlorhydria. Of the remaining 5 cases, 1 showed no secretion of free hydrochloric until after one hour and 2 showed a temporary high peak in the curve of acidity, with an abrupt fall to the base line. Other features revealed by the test were a tendency to rapid emptying such as prevails in other cases of so-called achylia gastrica and a highly mucoid resting secretion, frequently of the viscid consistency of raw egg-white. The increased liability to acne rosacea during the menstrual period and pregnancy is of interest, in view of the fact that achylia is also reputed to be more common at these times. The administration of dilute hydrochloric acid, 30 minims and upward, well diluted, after meals or during meals, has yielded very satisfactory results.

Cutaneous Cancer. From a study of the clinical histories of patients, McCoy¹³ is convinced that cancers of the muco-cutaneous margin of the lip, or cancers commencing at that point, are in no way due to solar light. Further, the lips near the margin seem to be immune to the development of keratoses. He has never seen a keratosis at or near the lip margin. He also calls attention to the significant fact that while a large percentage of cutaneous cancers of the lip margin are of the cuboidal-cell type, cutaneous cancer of covered parts is quite rare and, when found, is nearly always traceable to rheumatism, while 37.7 per cent of all cancers, both deep-seated and superficial, have occurred on the face (exclusive of the lip margins), the hands and neck, parts exposed to solar light; and that they have attacked persons whose vocations or habits involved insolation to a considerable degree. McCoy agrees with Unna and others that insolation produces keratoses, and that these are the most frequent of precancerous lesions. Sixty-two per cent of his patients were blondes, 7 per cent were dark-skinned persons and 31 per cent were chatains, or persons having a skin only slightly pigmented. Inasmuch as the kera-

¹² Lancet, 1920, p. 2.

¹³ Archives of Dermatology and Syphilis, February, 1920.

tosis is an admitted precancerous lesion, McCoy advises that it should unfailingly be removed.

A clinical study of 122 cases of epithelioma of the lower lip is reported by Lain.¹⁴ These were classified clinically rather than pathologically into the following classes: Class I. Epithelioma which may begin as a seborrheic-like crust, a small recurrent vesicle or fissure, at first superficial, later becoming infiltrated and indurated, and situated entirely or almost entirely on the cutaneous surface of the lower lip. These lesions are generally of slow growth and late to metastasize.

Class II. Those which are so located that one-third or more of the lesion overlaps the muco-cutaneous border of the lip. In these cases early metastasis occurs in the glands of the deep maxillary regions. Routine attention to the lymph drainage of this class is advocated, however early or localized the lesions and regardless of the treatment pursued.

Class III. All cases in which more than half of the malignant growth is situated on the mucous surface of the lip of many weeks' or months' duration and cases which, owing to neglect or incomplete treatment, have had a marked recurrence. Glandular enlargement in this class is usually present. The prognosis by any known method of treatment is unfavorable.

In the 122 cases, 117 were men and 5 were women, the ages ranging from twenty-three to eighty-six years. Farmers and outdoor laborers were mostly affected. Treatment with the roentgen ray or radium, singly or combined, was given to 107 patients. Of 72 patients treated and belonging to Class I, 95.8 per cent are living or have lived for more than three years. Of 27 patients belonging to Class II, 70.3 per cent lived from one to nine years. In Class III, 19 patients were examined, of whom four were treated. Three of these died within one year.

Lain concludes that neither surgery, roentgenotherapy nor any other one successful method of treatment should be used in all cases alike, and that radium and the roentgen ray, singly or combined, give the most satisfactory results in a selected class of epithelioma of the lower lip.

THE ROENTGEN-RAY TREATMENT OF CUTANEOUS CANCER is discussed by Hazen.¹⁵

The following types are recognized: The malignant mole or melanoma, xeroderma pigmentosum, prickle-cell or squamous-cell cancer, the basal-cell cancer and the carcinomas arising from the various cutaneous appendages, namely, the sweat and sebaceous glands and the hair follicles. The most important varieties are the prickle-cell and basal-cell growths, and both pathologically and clinically they are totally distinct diseases, for the former always tends to form metastases while the latter never does; in addition the former grows more rapidly and more deeply and is comparable to cancer of the breast in the therapeutic problems presented.

The types of basal-cell cancer that may be recognized are: (1) Very superficial types which resemble psoriasis, the chief difference being

¹⁴ Journal of the American Medical Association, October 16, 1920.

¹⁵ Ibid., April 30, 1921.

that a few early nodules can be seen at the edge of the lesions; (2) the common superficial rolled edge type, usually with a superficial central ulceration, but occasionally with a fungus growth in the center; (3) deep ulcers; (4) the superficial nodular type; (5) deep nodules, which frequently take the form of infiltrated plaques; (6) the morphea-like type, which is really an indurated plaque, and (7) the cicatrizing type, in which there is a spontaneous healing in the center while there are nodules or even ulcers at the edge.

One hundred and four persons were affected and 147 basal-cell cancers were treated. Of these patients, 61 were men and 43 were women.

In 77 instances the cancer sprang from keratoses; in 11 instances from congenital warts or fibro-epitheliomas; in 3 instances from pigmented moles, and in 6 instances from constant slight trauma, almost invariably that produced by tightly fitting glasses.

The earlier cases were treated with a water-cooled gas tube, a Benoist penetrometer being utilized to measure the quality of the ray, and pastils and Holzknecht radiometer to measure the quantity; however, the vast majority were treated with a Coolidge tube and an interruptless transformer. The dosage employed was: Spark gap, $7\frac{1}{2}$; focal skin distance, 8 inches; time, $2\frac{1}{4}$ minutes; milliamperage, 4. This gives about two skin units. In none of the superficial cases was a filter employed, but, when there was a deep infiltration, 1 mm. of aluminum was generally used. As time has progressed there has been a tendency to make the first treatment at least rather heavier; for instance, in the early cases one and three-fourths minutes was practically the standard time, but for the last three years two and one-fourth minutes has been universally employed. Of course, when a filter was used the time was much increased. The interval between treatments depends on the amount of reaction. A second treatment is not given in the presence of a marked erythema; however, the average interval is three weeks. None of the cases were treated by a preliminary curettage.

In exceptional instances it was found that a 2-unit dosage failed to benefit a basal-cell growth, but a $2\frac{1}{2}$ unit accomplished this end.

No attempt was made to heal the lesion with one heavy dose. Hazen is of the opinion that two or three small doses are less likely to be followed by sequelæ than when one very heavy dose is used. Table I shows the number of treatments required to heal the lesions.

TABLE I.

Treatments.	1.	2.	3.	4.	5.	6.	Many.
Type of lesion:							
Superficial plaque . . .	2	3					
Rolled edge	3	37	17	4	2	..	2
Deep ulcer	1	1			
Superficial nodule . . .	2	3	15	4			
Deep nodule	1	4	2	1	4	3	
Morphea-like	1					
Cicatrizing	2				
Totals	8	48	37	10	6	3	2

The results of treatment are given in Table II.

TABLE II.

	Number of cases.
Well three years	16
Well two years	17
Well one year	39
	<hr/> 72
Relapses cured	4
Relapses healed	2
Healed	41
	<hr/> 119
Not cured	16

Of the 16 cases which did not respond to treatment, 6 were hopeless at the start—hopeless because the ear was deeply invaded—and none of these patients responded to radiation, although all of these were cured by the cautery. It is a fact generally observed that neoplasms which have involved the cartilage, either in the ear or on the eyelid, are difficult to cure either with the roentgen ray or with radium.

In the treatment of cutaneous cancer, the following agents are in vogue: Excision, destruction with electric cautery or with the following commonly used caustics, arsenic, chloride of zinc, pyrogallol, trichloroacetic acid, the application of the roentgen ray or radium.

The choice of method for the removal of cutaneous cancer cannot be stated arbitrarily. Hazen in the above review has obtained good results with the exclusive use of the roentgen ray. In a report some years ago by Sherwell,¹⁶ 90 per cent permanent cures in selected cases were obtained by the vigorous use of acid nitrate of mercury. Robinson claims to have cured at least 90 per cent with an arsenical paste. The method which in my experience has given excellent results, and is applicable in most cases, is curetting the growth under local anesthesia, and then its destruction by the electric cautery or the application of a caustic. Just after this procedure is carried out, the area is treated with a massive dose ($1\frac{1}{2}$ to 2 skin units) of the roentgen ray. In the majority of instances this treatment suffices. In some cases, however, this treatment is not the method of choice, for example, in epitheliomas near or involving the eyelids; in these instances, the roentgen ray may be used alone. In large cancers it may be difficult to remove with the electric cautery; in this event, after curetting, I apply a caustic paste. In a recent case treated—a cancer as large as an egg—the growth was cured, with excellent cosmetic results, by the use of a zinc chloride paste.

One objection to the exclusive use of the roentgen ray in the cure of cancer is that it involves a much longer time than if the growth is first destroyed by one of the above methods.

When a caustic paste is employed the thickness of the application depends upon the depth of the cancer. The paste is removed in twenty-

four hours, the inflammatory reaction is treated by bland applications and the wound is allowed to heal. The cosmetic results are good; the scar is soft and pliable.

Small epitheliomas involving the lip may be removed with the curette, followed by the cautery and the roentgen ray; when the growth is large, excision with a considerable part of apparently healthy skin is the method of choice. In these instances, if the lymph nodes are involved, and the same applies to prickle-cell cancer in any area, they should be removed by a block operation or treated by massive doses with radium or with the roentgen ray.

Radium is being extensively used at the present time in the treatment of skin cancer, but except in certain localities in which the roentgen ray is difficult of application there is no convincing evidence as yet of the superiority of radium over the roentgen ray.

PRECANCEROUS DERMATOSIS OF BOWEN. The outcome of 2 cases of this affection described by Bowen¹⁷ in 1912 and 1915 is reported by this writer. In 1 case twenty-nine years have elapsed since the beginning of the cutaneous affection and the patient has been practically free from lesions for several years, following active destructive treatment, although a tendency to recurrence asserts itself from time to time. In this case the lesions have always remained localized in a limited territory. In another case the patient died of internal cancer in May, 1918, thirty-four years after the first appearance of the skin affection, which in his case was much more widely distributed and more varied in type.

Precancerous dermatosis, although it cannot be advocated as an exact term, serves to call attention to the group of cutaneous affections which include Paget's disease of the nipple, xeroderma pigmentosum, keratosis senilis and arsenical keratosis, in all of which carcinoma results much more frequently than in other skin affections, and all of which have many points of histological resemblance. The cases under consideration belong in this category, at least for purposes of study, until a more scientific and exact classification can be offered.

Since Bowen's report, in 1912 and 1915, the subject has been studied by Darier in 1914, and in another more recent report by the same writer.¹⁸ Darier states that clinically the cancer is remarkable by its peripheral extension rather than by its extension in depth, and by its tendency toward the formation of vegetation and ulceration. It gives rise to circumscribed areas of conglomerated excrescences, separated by deep furrows which are covered by crusts and squames. Over the surface are disseminated white points which resemble grains of milium. The growth is sufficiently rapid so that in the course of a few months the cancer may involve the entire face. In the case under observation, persistent and rebellious hemorrhages occurred at frequent intervals. Unlike the basal-cell epithelioma, it gives rise to a regional adenopathy. The adenopathy is characterized by very small glands which are multiple and not conglomerated, and it differed in this respect from the adenopathy of the spindle-cell epithelioma. At a later stage it has a marked

¹⁷ Archives of Dermatology and Syphilis, January, 1920.

¹⁸ Ann. de Dermat. et de Syph., February, 1920.

tendency toward the formation of metastases. These metastases take place by the way of the lymphatic vessels, and eventually involve the lungs, the peritoneum and probably other viscera.

Histologically, this cancer is even more characteristic. It is made up of masses of atypical Malpighian epithelium. The cells are voluminous and frequently edematous and have nuclei which are unequal and of which a great number are of the giant type. Some are multiple or deformed and of monstrous size. These are the cells which have been described as "dyskeratosis." The center of these masses of epithelium sometimes undergoes a necrotic degeneration. The stroma of the tumor is fibrous, without any inflammatory reaction. The texture and the structure of the cancer is exactly the same in the skin, in the glands and in the visceral metastases. This structure is absolutely identical with that of the epidermis in the areas of dyskeratosis of the precancerous type described by Bowen, the areas in which the cancer develops directly. The only cancer with which this presents any histological analogy which might be called striking is that of the dyskeratosis of Paget, or Paget's disease of the breast. These two dyskeratoses, which are precancerous, are manifestly two neoplasms which are distinct one from the other. Further research is necessary to determine whether these two cancers which develop from the two dermatoses differ sufficiently to enable one to make a distinction either clinically or histologically.

The treatment of this cancer was not at all satisfactory. Intensive radiotherapy was begun early in the disorder, when the patient was first seen by Dubreuilh, of Bordeaux. Later at L'Hopital St. Louis intensive radiotherapy was likewise given without results. Darier is of the opinion that when this transformation is first observed, recourse should be had at once to surgical excision.

Ringworm. Hartzell¹⁹ reports the occurrence of *two unusual cases of ringworm*.

The first case occurred in a man, aged thirty years. The eruption was an extensive one covering almost the entire right deltoid region and a large part of the right half of the trunk. The eruption consisted of numerous papules and nodules varying in size from that of a hempseed to that of a split-pea. They were dark red, and, for the most part, discrete. They were most abundant about the posterior borders of large, moderately pigmented areas in which were a few scattered nodules and small superficial scars and many of them had small blood crusts on their summits. It was quite evident that the disease was slowly extending backward toward the spinal column, the pigmented parts representing areas over which it had already passed. According to the statement of the patient, and as was evident from the excoriated condition of many of the papules, the eruption was attended by severe itching. The patient's first statement as to its duration was that the disease had lasted three years, but further questioning brought out the fact that five years before there had been little rings on the chest which gave him no concern; only in the past three years had the eruption spread extensively and

¹⁹ Archives of Dermatology and Syphilis, January, 1920.

caused annoyance. In addition to the affection of the skin, the nails of the index, middle and ring fingers of the right hand presented marked evidence of disease. They were rough and lusterless, with ragged and broken free borders.

In scrapings taken from the skin and the nails, an abundance of mycelium presenting the morphological character of the trichophyton was readily demonstrated. No culture was made in this case.

The second case occurred in a man, aged twenty-eight years, who presented a number of dark red, slightly pigmented round and oval patches, varying in size from that of a coin to that of the hand, situated over the crest of the left ilium, in the pubis, on the buttocks, on the posterior surface of the thighs and in the left popliteal space, this region showing a patch quite as large as the hand. The margins of these patches were decidedly elevated and their surfaces were covered with a scanty, fine, bran-like scale. In addition to these patches there were a number of brownish-red nodules, the size of shot with a hard dark crust on the summit, scattered about on the posterior surface of the left thigh in the neighborhood of the large popliteal patch. The disease had lasted about eight months and was still extending. He complained of no subjective symptoms of any moment. A diagnosis of syphilis had been made by his former medical adviser, a genito-urinary specialist of considerable repute, and three or four injections of arsphenamin had been given, of course, without any effect on the disease. In scrapings removed from the diseased areas numerous mycelia were readily found presenting the morphology of the trichophyton, of which cultures were obtained, to which reference will presently be made. Under strictly local treatment, which, as in the former case, consisted of the application of a 2 per cent solution of salicylic acid in alcohol, the eruption rapidly disappeared, and at the end of three weeks nothing remained but a moderate brown pigmentation.

From studies of cultures made from the organisms found in the tissue of this case, Hartzell was of the opinion that the organism was probably *Trichophyton rosaceum*, an organism which in Sabouraud's experience is only rarely a cause of ringworm, eight times in a total of 800 cases of various dermatomycoses.

These two cases of ringworm are unique not only in clinical appearances, but in the duration and extent of the lesions.

Our knowledge regarding the clinical features of ringworm has been greatly enlarged in recent years. The scaly patches on the scalps of children which everyone associates with ringworm is only one of many clinical forms of this disease. Infection by the trichophyton and other nearly related fungi may produce dermatoses with variable features presenting none of the clinical features commonly associated with ringworm. Ringworm may appear as moist eczematoid lesions commonly seen between the toes and fingers, as dry, sharply circumscribed eczematoid lesions on flat surfaces as deep inflammatory lesions—kerion—or, as an eruption resembling, more or less, lichen scrofulosorum, the so-called lichenoid trichophytides of Jadassohn caused by the *Trichophyton profunda*.

Rasch²⁰ reports interesting clinical, cultural, immunological and therapeutic observations on "*kerion*."

Experiments with animals explain the long-known fact that the most severe form—*Trichophyton profunda* (*kerion*)—accompanied by inflammation and swelling, is most quickly and easily cured, while the "lightest," most superficial cases take the longest time. With the first occurs a complete change in the organism by the formation of an abundance of matter which secured immunity, whereas the latter affections, which are only found on the epidermis and in the hair, do not set up enough local reaction to produce the formation of this matter.

The author's cases show that with *Trichophytia profunda* several other eruptions occasioned by this disease are found in addition to Jadassohn's lichenoid eruption. During the years from 1912 until June, 1919, 109 cases of trichophytia have been treated in the hospital. Of these cases 72 were accompanied by kerion formation, and 51 were localized in the hair of the head and 20 in the region of the beard. Culture was undertaken in only about half of the cases. As regards the cases found in the scalp, *Trichophyton faviforme discoides* was found most frequently (13 times), *T. violaceum* grew twice, and *T. gypsum asteriodes* twice. No fungus grew from a number of the cases; most of these, however, are probably due to *T. faviforme discoides*, from which it is often difficult to produce cultures. As regards the cases in the beard, *T. faviforme discoides* was found 4 times, *T. plicatile* twice, the very closely allied *T. cerebriforme* twice, *T. gypsum asteriodes* once, and *T. rosaceum* once.

Granuloma trichophyticum (Majocchi) was found 4 times; in 2 of these cases successful cultures of *T. plicatile* were found.

In 19 of the patients (all children) the papular eruption, the so-called lichenoid trichophytides described by Jadassohn in 1911, occurred, sometimes combined with spinulous, vesicular or pustular formations. In 6 cases in which the fungus was grown, it was found to be the *T. faviforme discoides*. This eruption is extraordinarily varied in its distribution, quantity and grouping. Sometimes only single, small, pink, scattered, follicular papules are found on the body, extremities or the face; sometimes it covers the entire skin with thousands of individual lesions, while in between are found all transitions. Sometimes the papules are distributed without any visible order; at other times they are grouped more or less regularly. The so-called corymbiform formation, as described by Inga Saeves, was seen twice.

In addition to this papular lichenoid eruption the cases have shown that various other forms secondary to the kerion formation are also seen. Thus pure vesicular eruptions generally consisting of purulent vesicles the size of a pin's head were found 5 times. This eruption was found once in large groups on the buttocks, once on the toes and once distributed on the arms.

A scarlatiniform eruption was seen twice. Such scarlatiniform eruptions with kerion seem only to have been observed once before, for

²⁰ British Journal of Dermatology and Syphilis, November, 1920.

Jadassohn says that it may come to an eruption well-nigh resembling scarlatina, without, however, giving any history of the disease. These erythemas should be borne in mind when the differential diagnosis of scarlatina is being considered. They do not seem to be particularly rare, as in the author's 51 cases of kerion of the scalp they occur twice. No doubt they will always be accompanied, or, in the course of a few days, be succeeded by a positive trichophytin reaction.

Kerion celsi also seems to be capable of causing erythema nodosum, resembling nodes on the shin bones such as B. Bloch and L. Pulvermacher (1919) have seen with kerion patients who also had lichenoid trichophytides. No such case was found in this series.

The treatment of kerion consisted of boiled-water fomentations only, which were changed from four to six times in the twenty-four hours. Under this treatment pain and swelling quickly abate and in the majority of cases no other treatment is called for. Under the fomentation treatment all the cases healed in the course of from three to six weeks, and what is of importance both theoretically and practically, *all other foci of trichophytia on the skin disappeared simultaneously without any local treatment whatsoever.*

A trichophyton infection reported by Sutter²¹ is remarkable, inasmuch as the trichophytide was hematogenous and constitutional symptoms were produced. The patient was a girl, aged ten years, who had been in contact with horses having ringworm for some time. She developed ringworm of the scalp, which, in the course of about three weeks, became rapidly transformed into kerion celsi. During this time the regional lymph glands became markedly enlarged and the child lost appetite and weight. About two weeks after the development of the kerion the girl became quite ill and manifested prodromal symptoms resembling those of an infectious exanthem. She suffered from headache, vomited, and developed chills and fever. The temperature reached 39.5° C., and over the entire body a bright red scarlatiniform rash appeared. The prodromal symptoms, the high temperature and the rash made the diagnosis of scarlet fever seem most probable. There was marked generalized adenopathy and a palpable spleen. About twenty-four hours after the onset of the exanthem the temperature dropped to normal and the exanthem became transformed into a fine, papulo-follicular eruption which in places was confluent and developed scales simulating a seborrheic psoriasisiform patch. About this time an acute arthritis developed in a number of the large joints. Puncture of the lymph glands gave a pure culture of *Trichophyton granulosum*, which was the same organism recovered from the kerion celsi and from the follicular cutaneous lesions.

Lupus Erythematosus. The etiology of lupus erythematosus is still the subject of much discussion. Although many cases of the disease present evidences of tuberculosis, and the results of the most recent bacteriological studies lend support to the view that it is a tuberculous disease, yet conclusive proof in this regard is lacking.

Hartzell²² reports a case of lupus erythematosus which had resisted

²¹ Archives of Dermatology and Syphilis, February, 1920.

²² Ibid., October, 1920.

all the well-recognized forms of local applications and which promptly improved after the extraction of a diseased tooth. There was no bacteriological examination made, and hence the organism concerned is not known. In another case studied by Hartzell, no evidence of a focal infection could be demonstrated.

A few years ago Barber reported an extensive case of lupus erythematosus in which there was found in the feces *Streptococcus longus*. More recently the same writer²³ reports another case associated with an infection of the tonsils with *Streptococcus longus*. The tonsils were removed and a vaccine made from the culture of *Streptococcus longus*.

An injection of a dose containing 5,000,000 of the organisms was followed by a decided reaction in the patches of lupus erythematosus, and after a larger dose, one containing 10,000,000, an intense reaction followed, together with considerable constitutional disturbance.

The streptococcus in this case was found not only in the tonsils, but also in adenoid tissue. The complete removal of all the adenoid tissue and the institution of treatment with sensitized vaccine resulted in retrogression of all the lesions without any further active local applications.

Low, Logan and Rutherford²⁴ report autopsy findings with bacteriological studies of two cases of lupus erythematosus. In the first case the patient experienced acute attacks of the eruption accompanied by pyrexia. The autopsy in this case revealed fairly extensive chronic tuberculous lesions, but not any more extensive than are frequently seen in patients dying of other affections. A streptococcus was recovered from the heart blood which was regarded as apparently the same organism which was recovered by Barber from the feces and tonsils in his cases of lupus erythematosus.

The second case reported was treated with vaccine made from *Streptococcus longus* recovered from the sputum. Diseased teeth were extracted. This treatment resulted in marked improvement of the lupus erythematosus, and some patches were completely healed. The postmortem examination revealed no macro- or microscopic evidence of tuberculosis.

In regard to the work of Barber one should be reserved about accepting any direct relationship between the streptococcus and lupus erythematosus *per se*. Some years ago I made cultures of the throats of 100 patients with scarlet fever, and these were bacteriologically studied by the late Dr. Gildersleeve, who found 92 per cent streptococcus in these throats. Cultures were then made from 100 apparently healthy university students, in whom 82 showed the streptococcus, and these killed guinea-pigs with as much rapidity as those from the scarlet fever patients.

In regard to the improvement which occurred in one of the reported cases of lupus erythematosus from vaccines it was possible that this was the effect of a non-specific protein. It is well known to dentists that the exacerbation of symptoms for which the patient sought relief often temporarily followed the extraction of incriminated teeth. This is

²³ British Journal of Dermatology and Syphilis, October, December, 1919.

²⁴ Ibid., August-September, 1920; *ibid.*, November, 1920.

believed to be due to the absorption of organisms from the vascularized infected focus. It is conceivable that an absorption of non-specific organisms might also bring about improvement.

Influence of Endocrine Glands on Skin Diseases. Pulay²⁵ deduces from what has been published on the relations between the skin diseases and the sexual glands that there is no evidence of any direct connection between disturbances in the genital sphere and abnormal conditions in the skin, with the exception of certain anomalies in the growth of the hair. He cites also the falling out of the hair sometimes noted with uterine fibromyomas and the rapid growing in of the hair again after these tumors have been removed, also the subsidence of seborrhea during pregnancy. On the other hand, the mineral metabolism has undoubtedly something to do with skin diseases. Morse found that ovarian treatment of castrated animals induced pronounced diuresis while phosphorus content of the urine declined. Matthes found increased elimination of phosphorus and lesser output of calcium and magnesium salts under ovarian treatment; after castration the output of each was increased. These findings suggest that ovarian treatment might modify certain dermatoses by its influence on the calcium and magnesium metabolism. Ischovezco has also apparently established that all organs rich in lipoids, like the endocrine glands, are stimulated to extrafunctioning when lipoids from the same organ are incorporated. He injected rabbits with lipoids from the uterus and noted that the uterus became hypertrophied. He also noticed an antagonistic action between lipoids from the corpus luteum and from the suprarenals.

The possible relation of the internal secretions to the skin and its appendages is also discussed by Oyarzabal. He cites a case of scleroderma developing in a girl, aged eighteen years, at which time menstruation stopped. The reports of other writers who have noted the relative frequency of scleroderma with symptoms of the menopause are mentioned. (In my experience scleroderma has not been notably associated with cessation of menstruation.—S.) Sabouraud's theory that alopecia is traceable to the excessive internal secretion of the sexual glands is cited. In seborrheic alopecia the secretion of sebum is excessive, and this does not occur until the sexual glands are developing. "Children never have seborrhea." The question of the relations between the endocrine and the sebaceous glands may repay study, and may throw light on baldness. Organ-extract treatment is justified in all cases of skin diseases or appendages in which endocrine deficit is suspected. Favorable results have been reported with mesenteric gland extract in the treatment of scleroderma and others with epinephrin in erythromelalgia. Oyarzabal cites a case of vasomotor disturbances in the hands and feet which existed for twelve years and which subsided under suprarenal treatment.

We have no definite knowledge of the rôle the endocrine glands play in the function of the skin and the causation of skin diseases. The relation between these glands and skin diseases is based upon theoretical

²⁵ *Therapeutische Halbmonatshefte*, June 1, 1920.

considerations and deductions. For example, acne most commonly develops at puberty and is accentuated at the time of menstruation. This association suggests a relation with the sexual glands. The dry skin of myxedema carries with it the thought that the thyroid gland may play a rôle in the causation of ichthyosis.

The above considerations form the basis of the employment of organo-therapy in skin diseases. The endocrine glands have been used notably in cutaneous diseases in which the etiology is as yet undetermined: for instance, acne, vitiligo, alopecia, scleroderma and ichthyosis.

Brilliant Green in the Treatment of Erysipelas.—Adams²⁶ advises the use of brilliant green in the treatment of erysipelas. The affected area is painted with a 5 per cent aqueous solution once a day in mild cases and twice a day in severe cases. This is applied without a dressing. When the eruption has subsided the discoloration can be removed in three or four days by vigorous washing, preferably with ether soap.

In studies conducted some years ago by Krumwiede and Pratt,²⁷ and more recently by Kolmer, Wood and Yagle,²⁸ brilliant green was found to possess high bactericidal activity for *Bacillus diphtheriæ* and such pathogenic cocci as staphylococci, streptococci and pneumococci. The clinical use of a 1 to 250 solution of the drug in water may prove of value in the local treatment of infections caused by these organisms.

Psoriasis. Clinical and radiographic examination of the lungs in 49 cases of psoriasis were made by Levy-Franckel and Jacob.²⁹ Of the 49 cases, 15 were found to be free from tuberculosis, 27 showed definite lesions and 6 showed very mild or doubtful lesions. From these figures Levy-Franckel and Jacob are of the opinion that a tuberculous soil is favorable to the development of psoriasis.

Many of the French school of dermatologists incline to the opinion that there is an etiological relation between tuberculosis and psoriasis. In this regard Milian reported some time ago obtaining reactions analogous to those in tuberculosis in a psoriatic by the injection of tuberculin. My experience does not warrant the belief that tuberculosis plays any role in the causation of psoriasis. On the contrary the disease is usually seen in those who are apparently in robust health. Indeed, psoriasis has been referred to as the "disease of the strong." The direct cause of psoriasis is unknown.

THE TREATMENT OF GENERALIZED PSORIASIS. Mook³⁰ reports obtaining good results in the treatment of generalized psoriasis from the following treatment which was employed in a British skin hospital in France:

Owing to the danger of chrysarobin dermatitis, as well as the destructive action of chrysarobin on clothing and bed-clothes, confinement to a room or hospitalization is necessary. Three ointments are used, the amounts of the drugs to be varied to suit individual reactions and idiosyncrasies.

²⁶ British Medical Journal, November, 1920.

²⁷ Journal of Experimental Medicine, 1914, xix, 501.

²⁸ Journal of Infectious Diseases, February, 1920.

²⁹ Bull. Soc. franç. de dermat. et de syph., 1919, p. 324.

³⁰ Archives of Dermatology and Syphilis, October, 1920.

In the treatment of the scalp, face and hands, salicylic acid and white precipitate of mercury, 5 per cent each, in white petrolatum is used daily. The percentage of the drugs may be increased continuously. If lesions exist on the hands or face, half of these strengths may be used. Tar ointments may be used in patients with an idiosyncrasy to mercury.

In the treatment of the body, two ointments are necessary—one to prevent as much as possible and to relieve the chrysarobin dermatitis. First a soothing application is used: 1 per cent ichthyol (or a substitute), cornstarch and zinc oxide, 6 per cent each, in white petrolatum. This is to be applied to the normal skin between patches before the chrysarobin ointment is applied. It is also to be used after the chrysarobin dermatitis has developed. Second, a chrysarobin ointment, which consists of 2 per cent phenol and 10 per cent chrysarobin in white petrolatum, is applied. These amounts will be advantageous in a majority of cases, but may be decreased or increased when advisable. The patient should be warned of the danger of conjunctivitis from chrysarobin and instructions given to prevent its occurrence.

After the ichthyol or soothing ointment has been applied to the normal skin between the lesions, preferably with a wooden tongue depressor or spatula, the chrysarobin ointment is applied to the lesions with a swab made of cotton or gauze twisted on the end of a stick. Stiff brushes are to be avoided as too irritating. Cornstarch or talcum powder is then dusted plentifully over the entire body and the patient advised to abstain from walking or exercising as much as possible, though it is not necessary to remain in bed.

Applications are made once daily until the chrysarobin dermatitis begins to develop, and it is at this point that the greatest skill in the treatment must be employed. The chrysarobin must be discontinued if severe reaction develops. An occasional cornstarch and soda bath may be advisable as a rest and for cleansing purposes, using two cups of cornstarch and one cup of baking soda to the bathtubful of warm (not hot) water.

The skin will be discolored after the first treatment, and after three to six days the skin generally becomes much reddened, but with less real inflammation than is usual when chrysarobin alone is used. The ointment is not to be discontinued unless the distress from burning and pruritus is unbearable. If the chrysarobin must be discontinued for a few days, the soothing salve is applied twice daily until it may be resumed. In some patients the chrysarobin may be applied continuously until all lesions have disappeared. In some patients two applications daily are possible, but in a majority rest is indicated after five or six days. Occasionally persons with idiosyncrasy will be encountered, and in these the method is useless.

In the treatment of psoriasis, the following considerations should be borne in mind: There are three stages in the disease—the developmental, the quiescent and the stage of spontaneous decline. If the disease is treated in the active developmental stage with arsenic internally or chrysarobin externally these drugs commonly cause a spreading or

extension of the eruption. In the quiescent stage of the disease these drugs have a marvellous effect on the eruption.

To convert the developmental stage into the stage of quiescence, the two following procedures are of value: First, the use of a low protein diet, and second, the administration of autoserum injections.

Studies of the Etiology of Xanthoma Multiplex. The results of an examination of the cholesterol content in the tissue and blood from a case of xanthoma multiplex are reported by Burns.³¹ In the examination of the blood for cholesterol as well as fatty acid, the method of Blow was employed. Cholesterol was found in large quantities in three of the nodules examined. The cholesterol blood content was found to be considerably increased under normal mixed diet, under low fat diet and under high fat diet. From the findings it would seem probable that Xanthoma multiplex is a dermatosis whose origin lies in increased cholesterol in the blood, the skin lesions of which are caused by its deposition where it induces a peculiar secondary connective-tissue hyperplasia.

The results of a chemical study and histological examination of a generalized case of xanthoma is recorded by Queziat and Laroche.³²

Histologically, there were found occasional islands of infiltration deep in the derma and surrounded by a very slight inflammatory reaction. There was noted in particular the entire absence of xanthoma cells of the classical multinucleated type. Examination with Sudan III, however, showed marked infiltration in the derma and a few rare globules of neutral fat. The lesion was remarkable because of the infiltration and because it lacked the inflammatory reaction usually present in xanthoma tuberosum or in xanthelasma. Chemical examination showed the lipoid infiltrate to be cholesterol. Examination of the blood showed only a slight increase in the cholesterol. This, however, probably is to be explained by the fact that only one examination of the blood was made. Had a series of examinations been made the hepatic coefficient of Amberg would probably have been demonstrated. There was no demonstrable hepatic lesion. The hepatic insufficiency was probably only functional and limited to the metabolism, and did not in any way concern the albumin metabolism.

In view of the hypercholesterolemia present in patients with xanthoma and the association of this disease at times with diabetes, it appears that the disease is due to pancreatic and possibly hepatic metabolic disorders. Indeed, Chauffard and Laroche state that xanthoma is a sign of lipolytic insufficiency of the pancreas. Owing to the hypercholesterolemia a low cholesterol diet should be administered.

Paget's Disease. A case of extramammary Paget's disease was reported by Satani.³³ The patient was a man, aged seventy-four years, who has a lesion in the right axilla with the same clinical and histological features shown by the lesion when it occurs about the nipple. In the middle of the right axilla was found an irregular, ovoid, flat lesion 7 cm. in long diameter. The margin was sharply defined against the normal

³¹ Archives of Dermatology and Syphilis, October, 1920.

³² Bull. Soc. franç. de dermat. et de syph., 1920, p. 208.

³³ British Journal of Dermatology and Syphilis, April, 1920.

skin and was elevated and slightly rolled. The surface of the patch was covered with granulations and superficial fissures, especially in the posterior quadrant, causing this section to have much the appearance of the brain surface. Some sections of the center and the top of the wart were slightly eroded and the entire center was of a deep red color, small portions of which were covered with thin brownish crusts.

When Paget, in 1874, first described this affection it was thought that the disease occurred only about the nipple. However, since this time other cases have been reported occurring on the back, the arm, the scrotum and penis and the buttock. In 1910, Hartzell collected 18 cases of extramammary Paget's disease, in which 9 were situated on the external genitalia or in regions immediately adjacent thereto, and 5 of these 9 were situated on the glans penis.

Extramammary Paget's disease does not differ from the disease as found on the breast.

Experimental Pellagra in White Male Convicts. Goldberger and Wheeler conducted this investigation at the Rankin farm of the Mississippi Penitentiary on 11 convicts who volunteered for the test. Those chosen had no previous history of pellagra either in themselves or in their families. The volunteers were placed on shorter work hours and had regular rest periods, their work being in the fields and classed as moderate or light.

The observations extended from February to October. There was no change in food until April 19, but the diet was restricted after that date. The average intake of each patient varied from 2500 to 3500 calories, 41 to 54 gm. of protein, 91 to 134 gm. of fat and 387 to 513 gm. of carbohydrate. The diet consisted of highly milled wheat flour, maize meal and grits, cornstarch, white rice, cane sugar, cane syrup, sweet potatoes, pork fat, cabbage, collards, turnips, turnip greens, coffee, "Royal" baking powder, salt and pepper.

None of the control patients developed pellagra, although in contact with it, while 6 of the 11 experimental patients developed evidence of this disease, the first symptoms appearing during the second month of the test diet. These symptoms were weakness, abdominal discomfort and headache. Loss of weight became marked in the last few weeks of the experiment. Six of the 11 developed skin lesions, beginning about five months after the institution of the diet, the first lesions beginning on the scrotum; later lesions appeared on the hands in one case and on the neck in another.

The authors consider that these 6 patients developed pellagra as a result of the experimental diet, and they emphasize the early development of the scrotal lesion, which appears to be much more common as an early symptom than has been previously recognized. They state that there may be certain qualities in diets which determine the initial dermatitis of an attack, these differences in quality corresponding to certain differences in clinical types.

They further state that the "dietary factors to be considered as possibly essential are: (1) Amino-acid deficiency, (2) faulty mineral supply, and perhaps (3) an as yet unknown (vitamine) factor."

The Histogenesis of Molluscum Contagiosum. In last year's PROGRESSIVE MEDICINE, I reviewed a series of experiments, conducted by Wile and Kingery, directed toward a demonstration of the etiological agent of molluscum contagiosum. As a result of these experiments these authors showed that molluscum contagiosum is caused by a filtrable virus.

Kingery³⁴ has more recently carried out studies with the experimental lesions of molluscum contagiosum in the various stages of development. As a result of these studies it was demonstrated that the lesions are limited to the pilosebaceous epithelium.

There is an abundance of clinical and pathological evidence which demonstrates the existence of the analogue of molluscum contagiosum in fowls. The absence of pilosebaceous epithelium in the combs and the feet of the fowls and pigeons, where lesions of molluscum epithelium often occur, justifies the conclusion that the lesions of this disease can develop independent of pilosebaceous structures. Presumptive evidence points to the identity of molluscum contagiosum in man and molluscum epitheliale in the lower animals.

Final proof of the development of molluscum contagiosum from the surface epithelium, therefore, must depend on the establishment of the identity of these two conditions. This identity will be proved only by the successful inoculation of molluscum contagiosum into fowls and of molluscum epitheliale into human subjects. Kingery is now conducting experiments directed toward this end.

Actinomycosis and Vaccine Therapy. A study of 25 cases of this disease is reported by Colebrook.³⁵ There is no reliable method of detecting an actinomycotic infection in its early stages, *i. e.*, prior to the occurrence of suppuration. The slowly progressive, comparatively painless and indurated lesion may suggest the diagnosis, but one is at a loss to confirm it by blood examinations. However, when an abscess is about to be evacuated or with lesions actually discharging the diagnosis need never be long in doubt. All that is then required is to detect the sulphur granules in the pus and to determine their mycelial structure.

The following simple procedure is recommended for the detection of granules whenever their presence is in doubt: A few drops of pus are collected in a test-tube half-full of water and fitted with a cork. On vigorously shaking the tube all the elements of ordinary pus will be emulsified or at least reduced to fine shreds; if, however, actinomycotic granules are present they will not be broken up, and on holding the tube up to a light will be easily detected by virtue of their opacity as cream-colored spherical bodies of about $\frac{1}{2}$ to 1 mm. diameter, which quickly sink to the bottom of the fluid.

With the finding of granules a provisional diagnosis of actinomycosis can be made. For confirmation of the diagnosis it remains to verify the presumption that these granules are composed of Gram-staining mycelial elements, and, whenever possible, to identify the organism by isolating it in pure culture. For these purposes the granules are trans-

³⁴ Archives of Dermatology and Syphilis, August, 1920.

³⁵ Lancet, April 30, 1921.

ferred as required by means of a capillary pipette to the surface of a microscopic slide. Lightly crushed under a cover-glass and examined unstained with a low-power objective the characteristic "ray" formation of clubs will be seen between an outer shell of massed leukocytes and the inner core of the granule.

The table shows the site of the infection, the incidence in the two sexes and the ultimate issue of the disease.

Site of infection.	Number of cases.	Males.	Females.	Ultimate result.
Face or neck	10	7	3	9 recovered completely; 1 died.*
Thorax	8	5	3	7 died; 1 lost sight of.
Abdomen	6	1	5	5 died; 1 recovered.
Dorsum of hand	1	1	..	Recovered completely.
Total	25	14	11	

Seventeen of the 25 cases were young adults, 7 were older subjects and 4 were children between the ages of ten and thirteen years.

The outstanding feature of the pathological process in all the cases was the extension by direct erosion of contiguous tissues, particularly connective tissues, such extension was usually accompanied by a deep induration, often quite a "wooden" induration over a considerable area around.

In the cervico-facial cases, although the infection presumably occurs from within the mouth or pharynx, the suppurative process almost always develops outward toward the skin and seldom points in the mouth.

The treatment consisted of surgical measures—incisions for the evacuation of pus and curetting. In view of the tendency of the disease to spread by direct extension in contiguous tissue, repeated incisions and efficient drainage are of paramount importance in the treatment of the disease.

In addition to the surgical measures, vaccines prepared from strains of *actinomyces bovis* of human origin were employed, and most of the cases received, in addition, other vaccines corresponding to their respective secondary infection. Autogenous *actinomyces* vaccines were used in 11 cases and the remainder received the polyvalent stock vaccine prepared by Parke, Davis & Co. The treatment was commenced with 2 or 2½ million myceline fragments at intervals of five days. The quantity was gradually increased as guided by the progress of the patient. The best results were obtained with doses of 4 to 10 million fragments. In a few cases which did not improve on smaller doses the quantity was considerably increased—in 1 case to 75 million fragments—but without any apparent advantage. The only reaction noted was a rise of temperature which occurred in a few cases.

The usually advocated treatment with potassium iodide was found to be of no value.

* Death was due to cerebral abscess, resulting from direct extension of the disease through the skull.

Colebrook concludes that the treatment of actinomycosis by vaccines facilitates recovery when efficient surgical drainage of the affected tissue is secured and maintained; when, however, drainage is unsatisfactory the use of appropriate vaccines will not usually suffice to stay the progress of the infection. In some of the cases improvement took place so rapidly after the use of vaccines that there seemed to be no doubt as to the efficacy of this treatment.

Radium and Radiotherapy. The 1920 report of the Radium Institute of England contains much that is of interest. A consideration of principles, a review of data obtained from 80,000 treatments and free reference to work from other sources have been combined to formulate general laws and give some indications for departure from routine methods in special instances.

An outline of the physics of radium therapy is given; the strength of all apparatus used in treatment is expressed in terms of hydrated radium bromide, a salt with a radium element content of 53.6 per cent; a section is devoted to a brief description of the α , β and γ rays (emitted alike by radium salts and radium emanation in a proportion of 10,000 to 100 to 1) and of the reflected and emergent secondary rays, the latter necessitating careful elimination on account of their irritating effects upon tissue. Clinical experience has led to definite limitation of the thicknesses of the various metals used for screening; the range lies between 0.01 mm. aluminium and 2 mm. lead.

Radium rays impart to living tissues a stimulus varying with the character of the rays and the period and extent of their absorption; pathological cells are more susceptible than normal cells and different varieties of cells react differently to radiation of given wave-lengths. It has been shown that cells are most susceptible when in a state of active nuclear division. The speed and power of α and β rays are gradually reduced in their passage through matter and finally disappear, but complete absorption of the hardest γ rays never occurs. The action of radium rays on various tissues and organs of the body has been carefully studied by many observers and a summary of the more important results is given in the report. Thus the changes induced in an area of skin subjected to irradiation are: (1) Epidermal proliferation, followed by desquamation; (2) congestion of the dermis, with destruction of hair follicles and sebaceous glands; (3) fibrosis; and (4) regeneration of hair follicles and sebaceous glands. In the blood a rapid increase of red corpuscles has been noted, persisting for some time and associated with a short leukocytosis followed by a marked leukopenia. The normal thyroid gland is but little affected by radium rays, although arrest of its secretory function, brought about by frequent and prolonged radiations with resultant fibrosis, has been recorded. With reference to the testes and ovaries, the seminiferous tubes and Graafian follicles are extremely susceptible and degenerate rapidly under radiation. Sterility has been specially observed in unprotected roentgen-ray workers, and hard roentgen rays are analogous to the rays of radium.

For the specific treatment of diseases certain fundamental principles are enunciated, and it is laid down that the effect of radium irradiation

on the living cell shows three clearly established phases: (1) Increase of cell activity, with possible associated proliferation; (2) arrest of cell activity; (3) degeneration and destruction of cells. The transition from stimulation to destruction is simply one of degree—no hard-and-fast line can be drawn between the phases. Details of treatment are then discussed under the headings of Malignant and Non-malignant Diseases—the former comprise the carcinomata, sarcomata, rodent ulcers and endotheliomata and the latter include fibromyomata of the uterus, leukocythemia, exophthalmic goiter, tuberculosis, nevi, keloids, lupus erythematosus, leukoplakia and warts, keratomata and papillomata. Reference is made to the publication of a paper dealing with the blood of workers at the institute,³⁷ in which are described 3 deaths of radium workers—2 in England and 1 in France. In 2 cases these deaths were ascribed to aplastic pernicious anemia; in the other the blood condition was similar, but the case was complicated by signs of infective endocarditis. Anemia of pernicious type was found in several other workers, and it is concluded that exposure to radium was in these cases the important etiological factor. The increased protection now afforded is already resulting in a return to normal of the blood of these workers.

The important monographs and papers on roentgenotherapy that appeared in Germany during the war are summarized by Solomon.³⁸ He states that filtered treatment for skin diseases amenable to radiotherapy seems to be in vogue. Much higher voltages are used in Germany than in this country. The aim appears to be to develop a homogeneous ray, as it is believed that its value is greater than a heterogeneous one. This applies to deep therapy, yet cannot be neglected in superficial conditions.

Several authors cite clinical experiences with filtered treatment (4 mm. aluminum) in skin diseases. Wetterer found that hypertrichosis, eczema of the face and sycosis responded better to the filtered ray. In the not too inveterate cases of acne vulgaris filtered rays give an ideal result. It is equally valuable in acne keloid. According to this author juvenile warts are rapidly healed by this method. However, in chronic eczema and psoriasis unfiltered treatment is more efficacious. Gunsett has obtained such excellent results in hypertrichosis by filtered therapy (4 mm. aluminum) that he believes that electrolysis will be superseded by this method of treatment.

On the experimental side, German investigators have come to some conclusions, already propounded in this country, anent the properties of the roentgen ray. For instance, Kronig and Friedrich, who have published a monograph based on their extensive experiments, declare that the biological effect depends on the quantity and not the quality of the ray absorbed. The intensity of the biological action for the same dose does not differ if the rays are unfiltered or filtered through 3 mm. of aluminum or 1 mm. of copper. Of particular interest is their conclusion that the intensity of biological action differs if the total dose is given at once or divided into fractional doses.

³⁷ Archives of Radiology and Electrotherapy, December, 1920.

³⁸ Journal de radiol. et d'électrol., 1920, p. 4.

PHYSICS OF ROENTGEN RAY. Shearer,³⁹ Professor of Physics at Cornell University, discusses the physics of the roentgen rays and the method of determining the dosage. The electrical conditions of operation fix absolutely the radiation delivered per second by a given target; hence adequate control of these conditions will enable complete duplication of radiation both in amount and quality. The two factors to be noted are: (a) Spark gap or tube voltage; (b) current in milliamperes. Of these, the former is by far the more important. The amount received by a given layer of tissue when the tube is operated for a definite time under prescribed electric conditions depends on two things: (a) The distance from the target; (b) the nature and thickness of all material through which the rays have passed before reaching the tissue treated. The reaction to roentgen rays by living tissue is due to rays absorbed, but there is no evidence at present that the biological effect depends on the particular wave lengths absorbed. The biological effect doubtless depends not only on the total amount absorbed, but to some extent on the rate of absorption; in other words, on the frequency of treatment as well as on the quantity of radiation. Layers of tissue near the surface of entrance always receive and absorb more radiation than the deeper layers. The inequality of absorption between deep and surface layers due to decrease of intensity with distance is reduced by increasing the distance of the tube from the skin. The inequality of dose between different layers is reduced by the use of filters. This inequality is also reduced by operating at a moderately high voltage.

Assuming that one desires to limit the effect as far as possible to a thin surface layer these facts would indicate a tube fairly close to the skin, operating at rather low gap and without filter. On the other hand, if one wishes to minimize the skin effect and secure more absorption in the deeper layers, the reverse would be true within reasonable limits; namely, greater target skin distance, higher spark gap and filtration.

Measurement of the surface radiation can be accomplished only by using some device to absorb all or part of the rays and show some observable change due to this absorption. Only a few such absorbers have been found, such as a photographic film or a layer of platino-barium cyanide crystals. Unfortunately, these indicators are troublesome for two chief reasons: (1) They absorb a different percentage of the total radiation for different voltages; (2) successive equal amounts of radiation absorbed do not give equal changes in the indicator. There is, therefore, no definite connection between their reading and the amount of radiation absorbed by the various layers.

The author believes that the physical side of this work and the apparatus should be developed to such a point that the therapist need have no doubt of his dosage and will not have to depend on any of the pastille or photographic methods of measurement. This will require coöperation and training, but would be amply rewarded by the increased usefulness and more extended application of this therapeutic agent.

³⁹ Archives of Dermatology and Syphilis, June, 1920.

THE TREATMENT OF KELOID WITH ROENTGEN RAYS OR RADIUM COMBINED WITH EXCISION. Pfahler⁴⁰ reports good results obtained in the treatment of keloid with roentgen rays or radium combined with excision. Pfahler points out that if the roentgen ray or radium is used early, when the scar begins to hypertrophy, there will probably be no need of combining excision with the radiotherapeutic effect. It is because of the frequent neglect of hypertrophied or growing scars that it is necessary to call attention to these methods of treatment.

When roentgen rays are employed, the aim should be to produce a progressive atrophy without erythema or destructive effect on the skin or overlying epithelium. The technic will vary considerably with the size or thickness of the keloid, especially in the cases in which the roentgen rays alone are used. The thicker and older keloids will require more filtration and correspondingly longer treatment. In recent cases of hypertrophied scars, in which the scar tissue is still quite young, considerably less treatment and less filtration is necessary. In these mild types one can use to advantage 5 milliamperes of current, 2 millimeters of filter with a focal distance of 8 inches, a parallel spark of 9 inches for a period of two minutes. This will give approximately 0.8 of an erythema dose and will be within safety limits. This treatment can be repeated in three or four weeks. It must be borne in mind that the factors given will vary in value considerably according to the instrument used, and one must familiarize himself with the value of each particular instrument. In the thicker and older cases of keloid which one is trying to eliminate by the roentgen-ray treatment alone, it is desirable when possible, to obtain a cross-firing effect. When this is possible the area to be affected is divided into two or more portals of entry, and the rays so directed through these various fields that the deeper portions of the rays will cross in the deepest portion of the tumor. In these cases it is desirable to use the following technic: 5 milliamperes with 6 millimeters of filter, a focal distance of 8 inches and a parallel spark of 9 inches for a period of eight minutes.

TREATMENT BY RADIUM. Radium will give very similar results if used in corresponding doses; that is, in the treatment of keloids one can produce results almost identical with those obtained from the use of the roentgen rays. Plaques or capsules may be used. One should learn the value of the particular specimen that is being used, and it should be used long enough to produce an erythema dose, with a filtration equal to approximately 0.5 mm. of silver. This will eliminate about 98 per cent of the beta rays. The duration of treatment will vary according to the size of the specimen used and the size of the keloid which is to be treated. In order to use the radium skilfully the value of the specimen over a given area with the filtration above mentioned at a given distance should be known. From this the necessary distance and area can be calculated according to well-known methods. A 50 mg. capsule with 0.5 mm. of silver and 1 mm. of rubber in direct contact will produce an erythema dose in one hour.

⁴⁰ Archives of Dermatology and Syphilis, August, 1920.

In the treatment of very large keloids and in small keloids in order to obtain a perfect cosmetic effect, Pfahler advises the combined use of excision and radiotherapy. MacKee was one of the first to practise this method of treatment; he advised excision and later treatment with radiotherapy. Pfahler, however, reverses this and applies the roentgen rays to the keloid area preceding the operation, preferably a few days to two weeks before, and of such a dose as one would give if the rays were to be depended on to remove the keloid. The keloid or hypertrophied scar is then carefully excised. This can be done best when there is sufficient loose tissue or skin around about to close the wound without too much stretching; the surgeon should excise as nearly as possible to the outline of the keloid and not attempt to excise wide of the area. Some surgeons unfortunately make a wide incision such as they would make when removing a malignant growth. This extensive excision only increases the area of scar tissue, for even though the keloid be excised there will always be a scar. The advantage of excision and combined anteoperative and postoperative roentgenotherapy or radiotherapy consists in the reduction of the scar to the level of the skin and in many instances of a decrease in the total area of the scar. Pfahler advises a full dose of roentgen rays within a week or ten days after the excision of the scar. The patient is then seen weekly, and if there is any tendency toward recurrence more treatment must be given. Three or four applications of the rays should be given to guard more certainly against a recurrence of the keloid.

The roentgen rays and radium are the only satisfactory treatment of keloid. In my experience excellent results have been obtained with these agents.

Syphilis. SACHS-GEORGI FLOCCULATION TEST FOR SYPHILIS. Many recent reports have appeared in the German literature on the Sachs-Georgi test for syphilis. An understanding of this test embraces the following considerations. Soon after the introduction of the Wassermann in 1906, it was shown that certain lipid substances, when used as an antigen, could replace the specific antigen composed of an extract of spirochetes (syphilitic liver), hence the Wassermann was no longer regarded as a genuine or specific antigen-antibody reaction. Further investigation showed that the reaction was of a physical nature and that the globulin fraction of the serum seemed to play an important part. It was also shown that syphilitic serums possessed, more so than normal serums, the property of providing precipitates when in contact with certain lipoidal emulsions. In the light of present knowledge, the Wassermann reaction may be defined as a reaction of a physico-chemical nature in which there occurs a precipitation of the globulin of the syphilitic serum by the lipoidal colloids of the antigen with absorption of the complement by this precipitate. It is thought that fixation of complement does not take place in the absence of such precipitation or flocculation, even though at the time the reaction takes place flocculation is not grossly apparent.

This understanding of the Wassermann reaction stimulated attempts to replace this complex reaction by one in which an obvious flocculation

would serve in its stead. Such flocculation tests were improvised some years ago, notably by Porges and Meyer, Herman-Peruty, Bruck and by Klausner. In these tests distilled water, solution of sodium glycocholate and cholesterolized glycocholate solutions were used. None of these tests offered a real substitute for the Wassermann reaction. The most recent and it appears the most successful test is that proposed by Sachs and Georgi.⁴¹

Technic. The lipoidal mixture employed by Sachs and Georgi is prepared as follows: An alcoholic extract of bullock's heart is made, using 1 gm. of heart muscle to each 5 cc of 96 per cent alcohol; 100 cc of this heart extract is mixed with 200 cc of 96 per cent alcohol and 13 cc of 1 per cent cholesterin (alcoholic solution). This cholesterolized extract is diluted with normal saline, just before the test, in the following way. To 1 volume of the mixture 1 volume of normal saline is rapidly added, and then 4 volumes of saline are added more slowly in such a way as to make an emulsion which is opalescent but not turbid. The serum of the patient is inactivated at about 55° C., the same as for the Wassermann test, and is then diluted 1 in 10 with normal saline, and to 1 cc of diluted serum is added 0.5 cc of emulsion prepared in the manner described.

In the original paper by Sachs and Georgi they recommended that the results should be read at the end of two hours' incubation at 37° C. Mandelbaum,⁴² Houck⁴³ and Amnenshauser⁴⁴ have shown that better results are obtained if the incubation is prolonged from eighteen to twenty-four hours. Sachs and Georgi,⁴⁵ in their second paper, have adopted this modification. A positive reaction is one in which there is a flocculation or precipitation visible to the naked eye.

Most of the German writers have used the agglutinoscope devised by Kuhn and Voit to read the results. A magnifying lens or even the ocular from a microscope can, however, be used with very satisfactory results if the tubes are held against a dark background. The flocculation may be very fine, smoky, finely granular, or may be precipitated at the bottom of the tube as a coarsely granular, flocculent mass. In a general way one can grade the degree of the reaction on a one- to four-plus basis.

In the performance of this test it is necessary that all glassware employed be scrupulously clean, otherwise falsely positive reactions may be obtained.

An idea of the clinical value of the Sachs-Georgi test may be obtained in the following reports:

Kumer⁴⁶ has performed over 2200 Sachs-Georgi tests, paralleling them with the Wassermann reaction. Eighty-one per cent gave identical results, and if those with minor differences were included the percentage of equivalent results reached 91. In his first series of 1245 cases there were 55 spinal fluids: 48 gave negative Wassermann and Sachs-Georgi

⁴¹ Med. Klin., 1918.

⁴² München. med. Wehnschr., 1918, 65.

⁴³ Ibid., 1920.

⁴⁴ Centralbl. f. Bakteriöl., 1920, 84.

⁴⁵ München. med. Wehnschr., 1919, p. 440.

⁴⁶ Wien. klin. Wehnschr., 1920, 33.

reactions; 2 gave positive Wassermann reactions and negative Sachs-Georgi reactions and 5 gave negative Sachs-Georgi reactions and weakly positive Wassermann reactions. Study of the history and clinical examination showed that the Wassermann reaction persisted longer than the Sachs-Georgi. The assertion has been made that the Sachs-Georgi reaction precedes the Wassermann in primary syphilis. The author had 44 initial lesions in the series; in 5 there was an agreement as to strongly positive, in 6 an agreement as to weakly positive and in 21 an agreement as to negative. In 1 case a positive Sachs-Georgi reaction paralleled a negative Wassermann reaction; 7 patients with negative Sachs-Georgi reactions gave positive Wassermann reactions, and in 3 cases the differences were not marked.

Kumer concludes that the Sachs-Georgi is a valuable reaction; it cannot as yet be substituted for the Wassermann reaction, but is the most desirable test to parallel the Wassermann.

Wodtke⁴⁷ states that the sensitiveness of the test can be increased by using double the amount of the serum prescribed, although with some serums this does not give as sharp a reaction as when the usual dose is employed. He also uses an additional extract of cholesterolized human heart and claims a higher number of positive reactions as a result.

Baumgartel⁴⁸ summarizes 25,000 tests made by others together with 7000 of his own, and states that the two reactions agree in 90 per cent of all cases. He recommends that the reaction be taken solely at incubation temperature and that the results be read at two, twenty-three and forty-eight hours.

Dekenga and Platenga⁴⁹ report occasionally conflicting findings, and state that the Sachs-Georgi test cannot be relied on alone, but in combination with the Wassermann test it may be of corroboratory value. They also state that the Sachs-Georgi reaction becomes negative sooner under treatment than the Wassermann.

Messerschmidt⁵⁰ finds the Sachs-Georgi of equal value with the Wassermann reaction in a series of 1100 tests.

The bulk of opinion in Germany has been in favor of the accuracy of the test. The amount of work on this reaction which has been carried on outside of Germany is, up to the present time, very small. However, Logan,⁵¹ Levinson and Peterson⁵² and Kilduffe⁵³ have recently reported on this test. Levinson and Peterson examined 1042 serums and spinal fluids with the Sachs-Georgi test paralleling it with the Wassermann test in 92 per cent of cases. In 62 cases in which the Wassermann test was negative while the Sachs-Georgi was positive or doubtful the clinical history or examination revealed evidence of syphilis in 58 per cent. Kilduffe performed the Wassermann and Sachs-Georgi tests in 296 cases. His conclusions are as follows: The Sachs-Georgi test is often difficult to read. It is not as delicate or as trustworthy as the Wasser-

⁴⁷ München. med. Wehnschr., April 2, 1920.

⁴⁹ Niderl. Tijdschr. v. Geneesk., May 8, 1920.

⁵⁰ Deutsch. med. Wehnschr., February 5, 1920.

⁵¹ Lancet, 1921, p. 200.

⁵² Arch. dermat. et syphil., 1921, p. 3.

⁴⁸ Ibid.

⁵³ Ibid., pp. 3 and 4.

mann test. It may be positive with Wassermann negative serums and negative with Wassermann positive serums. The number of non-specific reactions is sufficiently high to render the test unreliable as a means of diagnosis.

Although the technic of the Sachs-Georgi test is simple, and could easily be performed in one's office, its performance requires some skill, particularly in reading the less positive reactions. In addition, not every antigen prepared serves the purpose. Indeed, the preparation of the proper antigen is perhaps the fundamental factor in the success or failure of the test. The matter of the antigen is still under study as are other phases in the technic.

It is evident that the experience of a very large number of workers must be collected before a reliable estimate of its accuracy can be made, and the time has not yet arrived for the collection of this evidence. The test is a valuable aid in the diagnosis of syphilis. In its present state it should not be used to supplant the Wassermann, but rather to supplement it.

STRAINS OF SPIROCHETA PALLIDA. The possibility of the existence of strains of *Spirochetæ pallida* was first suggested by Noguchi in 1912 and later made the subject of experimental investigations by Nichols, Reasoner and others. Recently this idea has been emphasized by the experimental work of Levaditi and Marie⁵⁴ in connection with general paresis.

Levaditi and Marie report their biological study of *Spirochetæ pallida* obtained from the blood of a paretic and *Spirochetæ pallida* obtained from a syphilitic cutaneous lesion. The former was called a neurotropic strain and the latter a dermatropic strain. The testicles of rabbits were successfully inoculated and the two strains were carried through many transfers in these animals.

The two strains showed a difference in their incubation period, in the character of the lesions, the progress of the disease and its virulence.

The incubation period in rabbits of the dermatropic strain, ranged from fifty-five to ninety-four days, whereas the incubation period of the neurotropic strain ranged from forty-three to seventy-seven days.

The rabbit lesions produced by inoculation with the two strains were different both macroscopically and microscopically. The neurotropic strain produced a papulo-squamous chancre which microscopically appeared as an erosion with superficial ulceration, slightly infiltrated, with no vascular lesions. Spirochetes were found in the epithelial layers. On the other hand the dermatropic strain produced an indurated chancre which microscopically appeared deeply ulcerated and intensely infiltrated; periarteritis and endarteritis were present. Spirochetes were found in the deeper layers of the skin.

The two strains showed a striking difference in virulence. The dermatropic strain retained its virulence for the lower apes and anthropoid apes even after a large number of passages through the rabbit, tested during the years 1908-1914. Through the accidental inoculation of one

⁵⁴ Ann. de l'Inst. Pasteur, 1919, xxxiii, 741; Compt. méd. Acad. d. sc., 1920, clxx, 1021.

of the assistants in the experiments, the authors were able to demonstrate that it continued to be pathogenic for the human subject as well; the local lesions, however, in the latter were mild. There was no lymphatic enlargement and the Wassermann did not become positive until a long time after the inoculation.

The virulence of the dermatropic strain for paresis was then studied. Two paretics were unsuccessfully inoculated with this strain, which was pathogenic for the rabbit and apes and the human subject, through accidental inoculation. (Except in the very early stage of syphilis, superinfection with spirochetes obtained from any source is rarely successful.—S.)

Levaditi and Marie state that this experiment confirms Kraft-Ebing's observation that paretics who are carriers of spirochetes with cerebral or circulatory localization show a distinct cutaneous immunity to the dermatropic strain.

It was found that the neurotropic strain was avirulent for the ape when inoculated after a single passage through the rabbit; similar results were obtained from experiments on the human subject.

Of most significance were their results of crossed inoculation experiments. These showed that rabbits that had recovered from inoculation with the dermatropic strain were refractive to inoculations with this strain, but when inoculated with the neurotropic strain developed the lesion characteristic of the neurotropic strain. Converse experiments were carried out with similar results. These observations, therefore, justify the conclusion that there is a biological difference between the two strains.

The question as to whether or not syphilitics destined to develop tabes or paresis are contaminated at the onset of their syphilis by a special type of spirochete, or whether this special type, owing to its residence in the central nervous system, is created as the result of a progressive adaptability, is one that is not easily determined. While some of the observations cited (instance of conjugal neurosyphilis) seem to indicate an original contamination, the authors believe that the two hypotheses are not only perfectly compatible but rather tend to confirm the existence of a neurotropic strain. Among the numerous syphilitic germs morphologically similar but differing in virulence, which transmit syphilis in civilized countries, as the result of old infection, there are some which are distinguished by a special aptitude to localize in the central nervous system. This does not imply that they are incapable of localizing in the skin or in certain viscera or in the cerebrospinal fluid, otherwise we would not be able to understand their ability to be transmitted from one individual to another by the cutaneous, mucous or circulatory route (hereditary). But they do seem from the very start to have a weak reaction on the skin and the mucous surfaces, as is evidenced by the transitory symptoms and their mildness as seen in the future paralytics or tabetics.

The neurotropic strain, however, is very early transformed into one whose affinity for the brain and spinal cord becomes more and more marked and almost exclusive, in that the parasites live and thrive in

contact with the cerebrospinal substance. It is this type of spirochete which has been studied and compared with the dermatropic spirochete.

It also seems that the difference between the two strains is not so great at the time of the initial contamination as it is when the paralysis or tabes is fully developed. In other words the spirochete that later becomes neurotropic protects the human subject against cutaneous and mucous syphilis, while the parasite already neurotropic does not immunize the rabbit against the dermatropic virus. In short, the budding of so-called parasyphilis appears to be due to a special kind of contamination by a type or stock of spirochete with a more or less neurotropic affinity capable of adapting itself with ease to the cerebrospinal centers and able even to become transformed, after a considerable lapse of time, into a variety having definite and almost exclusive neurotropic characteristics. This neurotropic character, indeed, may be so definite that the lesions in the cerebral cortex and the spinal cord having in common with those generally considered by pathologists as characteristic of syphilis.

Since Levaditi and Marie's publication, a number of papers have appeared concerning the unity or duality theory of spirochetes. Judging from these reports, there are few partisans of the duality theory.

Sicard,⁵⁵ in an extensive report, states his objections to the duality theory. He admits that there are analogies with various organisms, particularly with the bacillus of tuberculosis and the bacillus of leprosy; but he is convinced that these differences in the bacilli are due merely to temporary changes due to their proliferation in different kinds of tissue and that essentially the bacillus is the same regardless of whether it has invaded the central nervous system or the skin.

If one admits that spirochetes have an exclusive affinity for the nervous system—in other words a neurotropic spirochete—these organisms could not be transmitted from one person to another except during the period of the chancre, inasmuch as the cutaneous and mucous lesions are, by the very definition, the extreme exception. Such an organism, therefore, is destined to disappear, because the opportunities for contagion are rare; but, as a matter of fact, syphilis of the nervous system is on the increase rather than the decrease.

Sicard's paper was taken up in detail in another paper published by Levaditi and Marie⁵⁶ in which they answered the objections made by Sicard. In this paper Levaditi and Marie reiterate the experimental evidence of the duality of spirochetes. They admit that there is only one variety of the syphilitic organism, but that there are two strains of this organism, a fact which is entirely in keeping with analogies of other organisms. They do not insist that the neurotropic organism invades only the central nervous system, and therefore there is no reason why that organism cannot be constantly carried from one individual to another. They do not maintain that crossed immunity occurs in man.

The unity and duality theories were discussed at a meeting of the Société française de Dermatologie⁵⁷ and at the Reunion Annuelle de la

⁵⁵ Presse méd., 1920, p. 513.

⁵⁷ Bull. Soc. franç. de dermat. et de syph., June, 1920, p. 183.

⁵⁶ Ibid., p. 646.

Société de Neurologie.⁵⁸ Many prominent dermatologists, syphilologists and neurologists took part in the discussion. Leredde, Sicard, Renault and Ravaut rejected the conception of the duality of the specific organism. On the other hand, Queyrat, Balzer, Milian and Jeanselme were inclined to accept it. Of the neurologists who took part in the discussion, the majority were inclined to attribute more importance to predisposing causes such as psychopathic inheritance, predisposition of the nervous system, alcoholism, trauma and circumstances intimately related to civilization as a cause of paresis rather than to a neurotropic strain of organism.

Of particular interest were the discussions of Shuzo Kure, of Tokio, and Weimaroyln, of Alexandria, Egypt. The former attested from personal observations as to the rarity of paresis in the Orient as contrasted with the Occident, whereas the latter spoke of the infrequency of paresis and tabes among the indigents of Africa. He mentioned frequently observing paresis and tabes among Europeans who had contracted syphilis from the native women. These observations were given as evidence against the conception of a neurotropic strain of organism as the cause of paresis.

The theory of duality of spirochetes should be entertained at the present time with reservation. The conception of a dermatropic and neurotropic strain of spirochetes is not entirely consistent with clinical observations of syphilis. It is quite possible, however, that after the spirochete invades the organism it may assume a dermatropic or neurotropic form, depending upon the predisposition of the individual.

The reported instances of conjugal neurosyphilis and of paresis developing in several individuals infected from the same source are arguments put forth by the partisan of the dual theory. As a matter of fact these instances are relatively rare and can, therefore, be used as an argument against the existence of a neurotropic strain. Moreover, the occurrence of paresis in the progeny of paretics is rare.

It is true one sees early and severe cases of neurosyphilis which run a rapidly fatal course, the "syphilis à virus nerveux" of Fournier. On the other hand, the majority of secondary syphilitics present spinal fluid evidence of an involvement of the neuraxis. Singularly, all of these individuals do not develop neurosyphilis as we see it clinically, regardless of this apparent involvement of the nervous system. It appears, therefore, that the spirochete is the *de facto* cause of neurosyphilis, and, in addition, there are predisposing and exciting causes. These causes are chiefly an outcome of the stress of higher civilization. Indeed, Kraft-Ebing's well-known dictum is to the effect that paresis is an outcome of the "syphilization of civilization."

There is a well-known dogma that neurosyphilitics rarely present clinical manifestations of tertiary syphilis involving other systems. This statement holds true clinically in the majority of cases, particularly of the skin and osseous systems, but less true of the visceral manifestations of tertiary syphilis, especially of the heart and aorta. Pathologically this dogma is less true than it is clinically.

⁵⁸ Ann. de dermat. et de syph., 1920, p. 465.

STUDIES OF LATENT SYPHILIS IN HUMAN SUBJECTS. In the study made by Engman and Eberson,⁵⁹ *Spirocheta pallida* has been isolated in 5 instances from latent syphilitic patients—3 times from inguinal glands (2 females and 1 male) and twice from the semen. The stains produced typical syphilitic lesions in rabbits' testicles and could be recovered and propagated for an indefinite number of generations. *Spirochetæ pallida* were isolated from patients who gave a history of syphilis dating back eleven and thirteen years in 2 instances and one year in 3 instances. An inguinal gland and the semen proved positive for spirochetes in the two first cases mentioned and the glands and semen in the last named. In this series of positive results a gland was found to be infectious in the case of a man whose Wassermann reaction had been negative, following treatment, and at the time of taking a specimen for the experiment gave 2-plus reaction in the cholesterin antigen only. A second instance of this nature was found in the case of a specimen of semen which proved positive for *Spirochetæ pallida*. It appears from this investigation and from that of others that the blood and other body fluids, excepting semen, are not infectious in latent syphilis, or if so, rarely. Incubation of blood from latent syphilitic patients did not favor any infectious property which might have existed. One-third of the total number of spinal fluids from latent syphilitic patients gave evidence of lymphocytosis, and one gave a positive Wassermann reaction. The groups studied were composed of untreated patients as well as of those who had received no treatment within the last two years. Between the time of taking specimens for inoculations of rabbits and the first symptoms or a suggestive history of syphilis in these patients from one to forty years had elapsed. Of a total of 500 cases of syphilis, 75, or 15 per cent were definitely latent. These investigations demonstrate the fact that those who give a history of a syphilitic infection may harbor active virulent *Spirochetæ pallida* for years, and this in the face of irregular negative Wassermann reactions or slight reaction in the cholesterin antigen only.

THE MARRIAGE OF SYPHILITICS. The Société française de Dermatologie et de Syphiligraphie⁶⁰ appointed a commission composed of Queyrat, Hudelo, Spillmann, Gastou and Simon to study the question of the marriage of syphilitics. The following report was submitted to the Society:

The syphilitic who marries takes the following chances:

1. Contamination of the wife or husband.
2. Transmission of syphilis to the children.
3. Bringing to the menage an altered health which may markedly diminish the social value of the individual; syphilis may shorten the longevity and may lead to visceral and especially to nervous complications.

With the present methods of treatment the risks of contagion are very slight because the lesions are promptly cured and rarely recur. The members of the commission are agreed that with sufficient treat-

⁵⁹ Archives of Dermatology and Syphilis, April, 1921.

⁶⁰ Bull. Soc. franc. de dermat. et de syph., p. 233.

ment the possibilities of contagion after the first year are very slight. The possibilities of a conceptional contagion, however, are quite different. They were not agreed on this point. The possibilities of contamination of the wife through the semen are well known. The work of Finger and Landsteiner are recalled, and in that work those men were able to get positive results with the spermatic fluid in 2 cases. In 1 case the donor had testicular lesions and in the second the testicles were clinically unchanged. Uhlenhuth and Mulzer also obtained positive results. Finally, *Spirochetæ pallida* have been found in the spermatic fluid, especially by Pinard. It is difficult to comprehend how an organism so large as the *Spirochetæ pallida* would infect the spermatozoön. It is possible, however, that a sporulating form, which would of necessity be very small, might invade the spermatozoön. Many syphilographers, of which the number is constantly increasing, deny the possibility of the mother being infected by the fetus. They insist that every woman giving birth to a syphilitic infant has been infected prior to the conception. The fact that the chancre has not been seen proves nothing. The benign character of syphilis of the so-called conceptional type may be explained by attenuation of the virus gained in the husband under the influence of treatment and of time.

The possibility of paternal heredity has been reduced to a minimum under modern therapy. Every syphilographer, however, has seen cases in which a patient armed with all the possible medical certificates of cure has married and has had syphilitic children. Moreover, it is a well-recognized fact that an old syphilitic without contaminating his wife may have offspring with various dystrophies, although the offspring may not have active syphilis. The dystrophies might be due conceivably to a toxic action on the spermatozoa by the spirochetes in the father.

Maternal heredity is of a much graver nature than paternal heredity. Every woman who has contracted syphilis prior to conception and who has active lesions will invariably give birth to a syphilitic infant. Moreover a woman who has an old syphilis which appears to be entirely inactive and who has had no signs for years may give birth to a syphilitic infant. In the opinion of the commission the question of the marriage of the female is a much graver one than the marriage of the male. This is a point which has not been brought out with sufficient clearness by the various authors. Practically all the authors have much to say about the husband but little or nothing about the wife.

The importance of maternal transmission is manifested in the following case I have recently observed: The husband and wife were syphilitics the duration of the infection was unknown; the blood Wassermann of both were 4-plus. There was a history of repeated miscarriages and still-born children. After twenty-five intravenous injections of arsphenamin administered to both hus' and and wife the Wassermann reaction of the hus' and remained 4-plus, that of the wife was negative. Soon after the time the Wassermann reaction of the wife became negative she gave birth to an apparently normal baby. The umbilical cord Wassermann at the time of birth was negative. The father's Wassermann at this time was still 4-plus.

The commission formulated the following rules:

1. If the patient has been seen and treated during the primary period before the appearance of the serological and secondary reaction and the patient remains free from positive serological and secondary manifestations during the first year, at the end of two years the individual may safely be allowed to marry.

2. If the patient is seen and treated after the appearance of the serological reaction, or even after the appearance of the secondary symptoms, and is given intensive treatment during the period of two years, and if the serological reactions, the urine reaction and the reactivation tests are negative and the spinal fluid is normal, one may safely at the end of two years allow this patient to marry.

3. If the seroreaction is persistently positive in the blood and the spinal fluid is normal, what is one to do? Would it be possible to continue this treatment until the blood becomes negative or should one allow the patient to marry? In the opinion of the commission, a persistently positive Wassermann reaction should not necessarily prevent the patient from marrying provided two conditions are fulfilled: (*a*) That the spinal fluid is negative, and (*b*) that the patient is a man. It is well known that men with persistently positive Wassermanns have married and have had perfectly normal, healthy children.

4. If, in spite of the energetic treatment, the blood reaction is either positive or negative, if the spinal fluid is positive one must be very careful about advising marriage. If, after energetic treatment, the spinal fluid becomes negative and remains negative for a few years one would be safe in permitting the candidate to marry.

5. If the patient presents positive signs of involvement of the nervous system one must absolutely insist that the patient shall not marry.

6. If the patient, an old syphilitic, is unable to give a definite and clear account of his infection and of his previous treatment one must be very cautious about giving him an opinion and, unfortunately, this is perhaps the most frequent situation in which the syphilographer finds himself.

Reference is made in the above report to the Wassermann reaction in the urine. The Wassermann reaction performed with urine is discussed elsewhere in this review.

The only safe and absolute criterion as to the time a syphilitic may safely marry is a persistently negative Wassermann reaction. It is true that men with a persistently positive Wassermann reaction may procreate healthy children, yet one cannot assure the patient that such will be the case. A long duration of infection in the husband and a negative Wassermann of the wife are factors which increase the likelihood of healthy children.

It is not definitely known how long a syphilitic may transmit the disease to his offspring. Instances have been reported in which transmission occurred as long as ten and twelve years after infection. Perhaps the first four years represent the time during which transmission is most likely to occur. After four years the probability of transmission becomes less likely and each succeeding year the possibility further decreases.

STUDIES OF THE URINE IN SYPHILIS. Simon⁶¹ reports obtaining a rather high percentage of positive Wassermann reactions in the urine of syphilitics. In some cases he obtained a positive reaction in the urine and negative reaction in the blood of the same patient. He is of the opinion that antisyphilitic treatment should be pursued until the urine gives a negative Wassermann reaction. He considers this just as important as the obtaining of a negative Wassermann reaction of the spinal fluid and the blood. In a second communication⁶² he gives the method employed in performing the Wassermann reaction with urine. A syphilitic liver antigen and an antisheep hemolytic system were used. The amounts of the different reagents used were measured in drops. The amount of urine employed in performing the Wassermann test was 10 drops. No mention is made whether the specimen was heated or unheated. Simon points out that larger amounts than 10 drops are often anticomplementary and that it is desirable to determine the anticomplementary dose of urine when used in performing the Wassermann reaction.

On the other hand, Klauder and Kolmer⁶³ state that, in their experience, it is the exception rather than the rule for the urines of syphilitic individuals to yield true positive Wassermann reactions. They performed the Wassermann reaction with the urine of 60 patients with syphilis in the different stages of the disease, many presenting acute symptoms and being untreated. Every patient yielded a positive blood Wassermann reaction, the majority of reactions being strongly positive with three different antigens. Of the 60 cases, the urines in but 2 yielded positive reactions.

Complement-fixation tests with urine are exceedingly liable to yield falsely positive results, owing to the highly anticomplementary activity of the urine. Anticomplementary activity varies with individual specimens. It is greater in old specimens than in fresh ones. Heating in a water-bath at 56° C. for thirty minutes removes only a slight amount of the anticomplementary substances.

Falsely positive results with urine are particularly likely if the amount used in the main tests is just under the anticomplementary unit. Under these conditions the control may show complete hemolysis, but the antigen tube slight inhibition of hemolysis, which may be interpreted as weakly positive fixation due to the presence of syphilis antibody.

Similar results may occur with the urine of healthy non-syphilitic persons, owing to the summation of the anticomplementary activities of antigen and urine in the antigen tube.

In performing the Wassermann reaction with urine, each specimen unheated was titrated for its anticomplementary unit and one-half this amount used.

The Wassermann reaction with urine may become a matter of importance in view of the fact that Simon advises that antisyphilitic treatment should be pursued until the urine gives a negative Wassermann reaction.

⁶¹ Bull. de l'Acad. de méd., 1920, lxxxiii, 73.

⁶² Simon and Lebert: Bull. de la Soc. franç. de dermat. et de syph., 1920, p. 117.

⁶³ Journal of the American Medical Association, 1920, lxxvi, 102-106.

In this connection it may be recalled that a negative Wassermann reaction of the urine was one of the requirements in determining the fitness of a syphilitic to marry, as given in the report of the French Commission already quoted. The highly anticomplementary activity of urine, as observed by Klauder and Kolmer, should be borne in mind when performing the Wassermann reaction with urine, otherwise falsely positive results will be obtained.

The report by Klauder and Kolmer is of further interest, since it contains much of clinical value. The urine was examined in 43 cases of untreated primary syphilis, the duration of which was from a few days up to the time of cutaneous manifestations. Urinary abnormalities were present in 3 cases. The urine was examined in 46 cases of untreated secondary syphilis. Urinary abnormalities were present in 4 cases. The positive cases all showed albumin and granular casts, excepting 2 cases in which casts were absent. In 2 cases red blood cells were present. The albumin consisted of a trace, except that in 2 of the secondary cases a light cloud was present with many granular casts and in 1 red blood cells. The urinary abnormalities disappeared after treatment with arsphenamin and mercury.

The urinary abnormalities in secondary syphilis are regarded as due in all probability to an invasion of the kidney by *Spirochetæ pallida* rather than due to syphilotoxins—which is the explanation usually given.

Clinical and experimental observations show that mercury is considerably more nephrotropic than arsphenamin or neo-arsphenamin. In the conjoined intensive treatment of mercury and the arsenicals, the nephrotropic action of mercury may retard the elimination of arsenic and in this way cause untoward effects of arsenic. In view of this possibility, conjoined intensive treatment with mercury and the arsenical preparations is not advised.

Spirochetæ pallida may be found in the urine of syphilitics in the acute stage of the disease.

There is no characteristic feature in the urine of paroxysmal hemoglobinuria of syphilitic origin which serves to differentiate it from the same condition due to other causes.

Results with urinary tests for syphilis were of no value as a means to the diagnosis of syphilis.

The kidney function of a series of syphilitic patients treated with arsphenamin injections was tested both before and after treatment with the phenolsulphonaphthalein test by Elliott and Todd.⁶⁴ The results of these experiments indicated that arsphenamin exercises very little influence on the kidney function. Experimentally, arsphenamin is considerably less nephrotropic, as shown in an extensive series of experiments by Kolmer and Lucke.⁶⁵

These studies are consistent with clinical observations that arsphenamin produces little or no urinary abnormalities even when employed intensively.

⁶⁴ Archives of Dermatology and Syphilis, December, 1920.

⁶⁵ Ibid., September, 1920.

The comparative effect of mercury and arsphenamin on the kidneys and the possible baneful influence of these drugs when administered conjointly and intensively will be pointed out in a subsequent section.

Silver Arsphenamin. The recent German literature contains numerous reports concerning the use of silver arsphenamin in the treatment of syphilis. Arsphenamin and silver in chemical combination—in the form of a sodium salt was suggested by Ehrlich, the synthesis of which was completed in 1918 by Ehrlich's pupil and successor, Kolle.

The rationale of the combination of silver with arsphenamin is the reduction of the arsenic dosage at the same time to reduce toxicity and to increase therapeutic efficiency.⁶⁶

Silver arsphenamin contains 22.4 per cent arsenic and 14.1 per cent silver. The arsenical content of arsphenamin is 30 per cent and of neo-arsphenamin 20 per cent.

Kolle⁶⁷ claims that, in contradistinction to other heavy metals, for example, copper, gold and platinum, silver in combination with arsphenamin has a special place in chemotherapy.

According to Kolle, the combination of silver with arsphenamin enhances its potency since such combination contains two chemotherapeutically effective components, silver having a catalytic effect on the arsphenamin molecule. He states that arsphenamin is a direct spirocheticide, because of the anchoring of the arsenic in the spirochetic plasma. Many experiments, especially those showing the slow disappearance of the spirochetes after the administration of this drug, incline to the opinion that silver acts as a restricting agent on the multiplication of spirochetes. The action of silver in silver arsphenamin is successful in preventing an increase of spirochetes because of the specific affinity of the arsphenamin to the spirochetes, and the silver with the whole molecule of the silver arsphenamin is anchored fast to the spirochetes of the syphilitic tissues. For this reason the combination of the silver with the arsphenamin is said to be of special chemical therapeutic value. The silver arsphenamin is alleged to act also on the spirochetes within the syphilitic tissue as a combination remedy in the sense that this term was used by Ehrlich.

The combination is stated not to increase the toxicity of the arsphenamin since it was shown in a series of experiments that the ratio of *dosis curativa* to *dosis tolerata* is 1 to 30. Certain experiments are said to demonstrate that silver arsphenamin is twice as effective as neo-arsphenamin. According to Kolle, the therapeutic dose of silver arsphenamin, 0.25 gm., has the same effect as 0.4 gm. of arsphenamin.

The structural formula of silver arsphenamin is not definitely known, particularly as regards the location of the silver in the molecule. It is thought by some that the silver is actually chemically combined and by others as finely divided or colloidal silver. On the other hand, Bauer⁶⁸ says that the silver in silver arsphenamin is not present in the oxide or colloid form, but in a complex combination that may be considered half colloid, on the boundary between colloid and crystalloid.

⁶⁶ Kolle and Ritty: Deutsch. med. Wchnschr., 1919, No. 18.

⁶⁷ Deutsch. med. Wchnschr., 1920, No. 2.

⁶⁸ Med. Klin., 1920, No. 4.

According to Bauer, the relative chemotherapeutic coefficient in silver arsphenamin is 1 to 25, in neoarsphenamin 1 to 10.⁶⁹ He further states that the arsenic component is materially decreased in silver arsphenamin owing to the combination with the antisypilitic silver component. A single dose of 0.2 gm. of silver arsphenamin contains 0.0254 silver and 0.043 of arsenic.

The drug is a grayish black powder which is dispensed in a sealed ampule. Solution of the drug is neutral in reaction, dark brown in color, and is less oxidizable than neoarsphenamin. If oxidized, the drug is toxic. In such an event the solution is not of dark brown color but is opalescent, or the powder floats on the surface of the water in black particles.

The dosage generally recommended is from 0.1 to 0.3 gm., and the intervals of treatment from twenty-four hours to four days. The number of injections is from eight to sixteen, according to the stage and the resistance of the disease.

The amount of solution for the intravenous administration of silver arsphenamin has been variably recommended by different writers. Kolle advises 10 cc of distilled water at warm temperature to each 0.1 gm.; others, however, use smaller as well as larger amounts. Some prefer administering the drug in 60 to 80 cc of normal sodium chloride solution.

The technic of administration, with a Luer syringe or a gravity apparatus, depending upon the amount of solution used, is essentially the same as for arsphenamin or neoarsphenamin. Most authorities emphasize the importance of giving the solution very slowly and attention is directed to the irritating effect of the drug on the tissues in the event of a faulty venipuncture. As with arsphenamin and neoarsphenamin, there is no standard treatment for the treatment of syphilis with silver arsphenamin.

Of the numerous writers on the use of silver arsphenamin, many have proposed a standard of treatment which differs in regard to dosage and interval of treatment. For example, Galewsky⁷⁰ considers small doses of silver arsphenamin necessary in the treatment of syphilis. He commences with 0.05 gm. of the drug for anemic women, otherwise 0.1 gm.; this dose is increased every four or five days to a final maximum dose of 0.3 gm. to men and 0.25 gm. for women. The total given by him to men in the course of treatment is 1.8 gm. and for women 1.5 gm. He ordinarily gives eight to fifteen injections in the first course of treatment for primary seronegative syphilis, and four to six injections in the after-treatment. In order to avoid what he terms spirochetal fever in virulent secondary stage syphilis, he gives a first dose of 0.05 gm. and second dose of 0.15 gm.

By spirochetal fever Galewsky doubtless refers to the fever sometimes accompanying the accentuation of the eruption which invariably appears

⁶⁹ In certain experiments carried out in the Dermatological Research Institute of Philadelphia, neoarsphenamin products have shown as high a chemo-therapeutic index as 1 to 40 or 50; in the same experiment the index for neoarsphenamin has been higher than for silver arsphenamin.

⁷⁰ München. med. Wehnschr., 1920, No. 5.

within twenty-four hours after the initial injection of one of the arsphenamin preparations when administered in the acute untreated stage of syphilis. This accentuation of the eruption and fever is called the Herxheimer reaction, and is generally considered as due to liberation of toxins resulting from the lytic action of arsphenamin on the spirochetes. Although the Herxheimer reaction in the above instance has not been proved to be harmful, yet it is generally stated that in order to avoid its occurrence the initial injection of arsphenamin should be small.

On the other hand, Dreyfus states that no fixed total dose has been found as yet. He has given as high as 3 or 4 gm. to a patient in from six to ten weeks without after-effects.

The interval between injections has been reduced by Arzt⁷¹ to twenty-four hours; he gives 0.15, 0.2 and 0.25 gms. on successive days, repeating the series four times at intervals of one week. Kolle⁷² warns against giving more than 2 gm. of silver arsphenamin in a month.

Insofar as the reversal of a positive Wassermann reaction and the rapidity with which spirochetes disappear from the chancre after the use of silver arsphenamin is concerned, it is doubtful if this drug is superior to arsphenamin or neoarsphenamin.

After an intravenous injection of 0.6 arsphenamin, I have observed spirochetæ to disappear from the surface of the chancre in from six to eight hours. In Lenzmann's⁷³ observations there was a decided influence on the spirochetes four hours after a dose of 0.1 gm. of silver arsphenamin, and within twelve hours practically no living spirochetes could be found; whereas Galewsky⁷⁴ states that within twenty-four to twenty-eight hours after an injection of silver arsphenamin the spirochetes are often not to be found in the local lesion.

In the eruptive stage of syphilis, the 4-plus Wassermann will usually become negative after the following treatment administered without mercury: Six to eight intravenous injections of arsphenamin or from twelve to sixteen intravenous injections of neoarsphenamin. In Hahn's⁷⁵ cases the Wassermann was always negative in fresh cases after twelve injections of silver arsphenamin, and nearly always negative in older cases. In those cases in which it was not negative, six more injections of silver arsphenamin were made without injury to the patient, and in some instances he went beyond that number, reaching twenty-four injections. In one-half of the cases treated by Hoffmann⁷⁶ with ten injections of silver arsphenamin, the Wassermann reaction remained positive. In Fabry's experience⁷⁷ the reversal of the Wassermann in some cases treated had not come up to his expectations. In 61 cases in the eruptive stage of syphilis reported by Walson,⁷⁸ in which 55 cases received silver arsphenamin and gray oil, 47 of these gave a negative

⁷¹ Dermat. Ztschr., 1920, No. 31.

⁷² Ztschr. f. arztl. Fortbild., George Speyer Hans, Frankfurt.

⁷³ Deutsch. med. Wchnschr., 1919, No. 13.

⁷⁴ München. med. Wchnschr., 1920, No. 5.

⁷⁵ Deutsch. med. Wchnschr., 1918, No. 50.

⁷⁶ Hoffmann, Veisser and Scholty: Deutsch. med. Wchnschr., 1918, No. 48.

⁷⁷ Deutsch. med. Wchnschr., 1918, No. 4.

⁷⁸ American Journal of the Medical Sciences, 1921, No. 141.

Wassermann in the first course, which consisted of seven treatments. The remaining 8 cases gave a negative Wassermann in the second course of seven treatments.

According to Galewsky⁷⁹ and to Gennerich,⁸⁰ the Wassermann reaction becomes negative sooner after silver arsphenamin than with the other arsphenamin preparations.

There is considerable controversy in the literature on silver arsphenamin, concerning the advisability, indeed, the necessity, of giving mercury in combination with silver arsphenamin. Wechselmann, Gennerich, Dreyfuss, Notthaft, and others, oppose the simultaneous injection, and Kerl, Goldberger, and others, sponsor the combination treatment. There has been much recent discussion regarding the conjoint treatment of syphilis with mercury and the other arsphenamin preparations. This phase of the discussion will be dealt with later. It may be mentioned here that since the introduction of silver arsphenamin, a new factor has entered the discussion. It is thought that the combination of silver and arsphenamin equals the mercury-arsphenamin combination. Moreover, the simultaneous injection of the three metals, mercury, silver and arsenic, would in all probability be too much for the organism to eliminate without causing damage.

All of the reactions incident to the administration of arsphenamin and neoarsphenamin have been observed following the use of silver arsphenamin.

A fatal case of hemorrhagic encephalitis following the use of silver arsphenamin has been reported. In Rieke's case,⁸¹ after the administration of 1.3 gm. of silver arsphenamin administered within forty-two days, dermatitis exfoliativa developed. Jaundice appeared twenty-four hours after the second injection of 0.2 gm. of silver arsphenamin in the case reported by Mueller. Most writers state that angioneurotic symptoms, the so-called nitritoid crisis, is a common phenomenon after the administration of silver arsphenamin, and some state that it is more frequent than after the use of the other arsphenamin preparations. Of vital importance is the possibility of argyria after the intravenous administration of silver arsphenamin. Such an occurrence has been reported by Lochte.⁸² A few days after the last of twelve injections of silver arsphenamin, the patient noticed the initial appearance of an ashen gray discoloration of the skin, which rapidly became more marked and progressed until the entire body presented a steel-gray color.

When one remembers that argyria is an indelible discoloration of the skin the treatment for which is of no avail, its possible occurrence following the use of silver arsphenamin even though extremely rare would lead to some reservation in the unrestricted use of this compound.

Because of the possibility of argyria, even though remote one, would hesitate to employ silver arsphenamin for an indefinite number of injections, such as is required in the treatment of neurosyphilis and in the resistant Wassermann cases.

⁷⁹ München. Med. Wehnschr., 1920, No. 5.

⁸⁰ Deutsch. med. Wehnschr., 1918, No. 45.

⁸¹ Med. Klin., 1919, No. 24.

⁸² Therap. Halbmonatsh., 1920, No. 34.

In conclusion, regarding this drug it may be said that it has not enjoyed a universal acceptance by those who have written concerning its use. In the opinion of Kolle (*loc. cit.*), Galewsky (*loc. cit.*), Hauch⁸³ and Gennerich⁸⁴ silver arsphenamin is better than any other arsphenamin preparation. On the other hand, Boas, Kissmeyer⁸⁵ and Muller⁸⁶ state that silver arsphenamin is the equal of arsphenamin. In Van Notthafft's⁸⁷ experience no better results were obtained from silver arsphenamin than with the other arsphenamin preparations.

A new drug is commonly heralded with great enthusiasm and is not infrequently credited with greater value than a subsequent and more extensive use warrants. In this respect one may recall Ehrlich's hope of accomplishing a "*therapia sterilans magna*" with arsphenamin when this drug was first employed in the treatment of syphilis.

THE SPIROCHETICIDAL VALUE OF SODIUM DIMETHYLARSENATE (MON-ARSONE). Major Nichols,⁸⁸ of the United States Army, reports the result of studies of the spirocheticidal value of mon-arsone conducted on syphilitic rabbits. He points out the chemical similarity of mon-arsone to sodium cacodylate; the former drug is disodium ethylarsenate and the latter drug is sodium dimethylarsenate. His previous study⁸⁹ of the spirocheticidal value of sodium cacodylate is quoted in which it was shown that this drug, even in toxic doses, had no effect on the spirochetes of syphilis. In spite of the history of sodium cacodylate, mon-arsone, a homologous drug, has been proposed as a substitute for arsphenamin and alleged to be less toxic and more parasitotropic than arsphenamin, although no evidence has been submitted to substantiate this claim.

Rabbits with chancres were treated intravenously with mon-arsone and examined daily for effects on the spirochetes and the lesions. As a result of this study it was shown that the spirocheticidal value of mon-arsone is too small to warrant any practical use of this compound in human syphilis. Indeed, it was shown that the tissues are fatally poisoned as soon as, or before, the spirochetes are affected.

The minimum lethal dose of mon-arsone was found to be 0.075 gm. per kilogram. The pictures, clinical and pathological, were strikingly uniform and consisted of somnolence and hemorrhagic tubular nephritis. The corresponding fatal dose for a 70 kg. adult would be 5.25 gm. The dose of 2 gm., which is advocated, is therefore closer to the theoretically dangerous point than is considered safe with other arsenicals. The corresponding minimum lethal dose for rabbits for sodium cacodylate is 0.15 gm. and for arsphenamin 0.1 gm. per kilogram.

Nichols states that in view of his results it is difficult to understand the claims that mon-arsone is an "ideal" arsenical compound for the treatment of syphilis. It lacks the essential characteristics of the arsphenamin group, namely, high spirocheticidal value.

⁸³ Med. Klin., 1919, No. 24.

⁸⁴ Deutsch. med. Wchnschr., 1918, No. 45.

⁸⁵ Med. Klin., 1920, No. 9.

⁸⁶ Deutsch. med. Wchnschr., 1918, No. 51.

⁸⁷ Ibid., 1919, No. 13.

⁸⁸ Journal of the Amer. Med. Assn., May 14, 1921.

⁸⁹ Journal of the American Medical Association, February 18, 1911.

A warning against the use in syphilis of new arsenicals which are not related to arsphenamin, and which are being sold with unwarranted claims as to their value, is aptly stated in an editorial in the *Journal of the American Medical Association*, February 26, 1921, and in a circular recently issued by the United States Public Health Service. In the latter circular attention is invited to the extensive exploitation through advertisements in professional journals and elsewhere of various arsenic preparations which are not related to the arsphenamin group.

In the opinion of the bureau, the subcutaneous, intramuscular or intravenous use of arsenic in the treatment of syphilis should be confined to the arsphenamin group, as these agents are now of established value and are produced under the regulations of the Public Health Service.

The employment in the early stage of syphilis of these various arsenic preparations, having little or no spirocheticidal value, is an injustice to the patient, inasmuch as valuable time is lost, since this period is the most appropriate one to cure the disease with one of the arsphenamins. It is therefore regrettable that these drugs with unwarranted claims are allowed to be sold through ill-informed loquacious salesmen to gullible physicians.

This entire subject can be summarized in the following way: There is at the present time no drug superior to the arsphenamins in the treatment of syphilis.

A Simplified Method of Preparing Solutions of Neo-arsphenamin has been described by Schamberg,⁸⁹ in which it is possible to prepare a solution of neo-arsphenamin for use without any other apparatus save a sterile glass syringe and needle and 5 cc of sterile distilled water. The glass ampule itself may be used to dissolve the contained powder. The technic of the method is as follows:

1. The ampule is shaken or knocked so that the powder flows easily and is not lumped.
2. The tip of the ampule is filed off. The opening should be large enough to permit the introduction of the needle to be used.
3. With the ampule almost in a horizontal position, 5 cc of sterile distilled water is introduced by means of the syringe.
4. The ampule is then agitated for from thirty seconds to a minute, when the powder should be in complete solution. To avoid spilling the solution, the finger, covered with a rubber glove or rubber finger-stall, should be held over the tip of the ampule.
5. The solution is then drawn up into the syringe and is ready for injection.

Experimental Syphilis in the Rabbit. A number of papers have been published by Brown and Pearce, of the Rockefeller Institute, in which they report various phases of experimental syphilis in the rabbit. Of the large number of papers which they published, only the ones will be reviewed that have interest from the clinical viewpoint of syphilis.

Their observations⁹⁰ on primary infection with syphilis in the rabbit's testicle are of interest in the clinical visualization of syphilis, and indeed

⁸⁹ *Journal of the American Medical Association*, 1920, lxxvi, 173.

⁹⁰ *Journal of Experimental Medicine*, April, 1920.

of all spirochetal diseases. The course of syphilis in the rabbit is somewhat a replica of this disease as observed clinically. Syphilis in the rabbit may be mild, transitory and spontaneously cured; again, the lesions may become quiescent or latent and later active; in this way a cycle is developed. As stated by Brown and Pearce, the duration of this local infection, as in experimental syphilis determined by the presence of active lesions, was as variable as the course of the infection itself, and no fixed limit can be given, either for the several phases of the local reaction or for the infection as a whole. The period of active infection varies from one to more than twelve months. In some animals the entire process was represented by one intense cycle of acute reaction, which terminated within from four to six weeks after inoculation; in others the infection continued through successive cycles of reaction, but the period of active infection was rarely longer than from two to four months. Brown and Pearce have also shown that *Spirocheta pallida*, just before the height or relapse of the acute cycle, began to increase in number. This increase continued parallel with the development of the lesions, so that by the time the lesions had reacted to the acme of the first cycle of their development, actively motile organisms were present in large numbers. At this point the organisms suddenly began to lose their motility and to collect in tangled masses; following this phenomenon they rapidly diminished in number so that within a few days organisms were difficult to find in fluid aspirated from the testicles, and those seen were either degenerated or showed slight motility; in many instances no organisms could be found. After passing through a crisis such as this, actively motile spirochetes again appeared in the testicular fluid and increased in numbers, thus presaging a renewed activity on the part of the lesions. These parallel changes continued throughout the existence of the local infection.

Brown and Pearce attribute the phenomena referred to above to a cyclical immunological reaction. They have further shown that the infecting power of the organism at this stage is greatly diminished. In one of their experiments a series of animals inoculated with approximately ten times the dose of immobilized and agglomerated organisms that was used in the controls showed an incubation period of six weeks as compared to three weeks in the controls, while the lesions were as slow to develop and were less pronounced than in control animals.

Similar observations as to the inactivity of *Spirochetæ pallida* at different periods of the infection were made, and there is no doubt in the minds of these workers as to the significance of the cyclical reactions they describe.

STUDIES OF LATENT SYPHILIS IN RABBITS. Brown and Pearce's⁹¹ studies on latent syphilitic infection in rabbits, with the demonstration of *Spirochete pallida* in lymphoid tissue, has a distinct bearing on latent syphilis in man.

In human syphilis there frequently comes a time during which the patient, although known to be infected, shows no obvious manifestation

⁹¹ American Journal of Syphilis, January, 1921.

of an active syphilitic process. Within recent years more exact clinical methods have shown that some of these patients are subjects of visceral or of nervous involvement, and are therefore cases of obscure rather than of latent infection. The work of Warthin has shown further that active pathological processes may exist where there are no clinical signs to indicate their presence, and finally that spirochetes with more or less tissue alteration may be demonstrated in individuals where there was little if any evidence either of disease or of infection. The number of cases of latent syphilis known and unknown is probably a very considerable one and is of increasing importance to the syphilographer.

Six rabbits which had recovered from generalized syphilis were used as the basis for determining whether such animals were still infected and something as to the location of the spirochetes in cases of latent infection.

One of the animals was inoculated four years and three months prior to the examination, another nine months and the others seven months. At the time the examinations were made, all of the animals showed a suggestive adenopathy which was most evident in the popliteal nodes. In addition, two of them showed slight lesions of an indifferent character in which no spirochetes could be demonstrated by dark-field examination. The others showed no lesions. The latent period of infection was of three months' duration in five of the animals and was six months in the other.

A popliteal node was removed from each of the animals and used for a test inoculation of two normal rabbits. Infection was produced in all cases, the incubation period varying from thirty-one to forty-four days, which is practically the same as that given by lymph-node inoculations during active stages of infection and shorter than that obtained from blood inoculations except in the most active stages of infections.

From these facts it may be concluded that rabbits which have recovered from clinical manifestations of syphilis may harbor virulent spirochetes almost indefinitely, even though no further manifestations of infection should occur. Moreover the infectivity of material from the popliteal nodes, taken in conjunction with other evidence of an affinity of spirochetes for lymphoid tissues, is interpreted as indicating that the lymphoid tissues of the body in general are probably the chief reservoirs of the virus during latent periods of syphilitic infection. From this it is suggested that a wider application may be made of our knowledge of lymphoid involvement in the management of cases of human infection.

The affinity of *Spirochetæ pallida* for lymphoid tissue has long been recognized; the adenopathy of syphilis is one of its most characteristic features. In like manner it has been shown, in all lesions, the points at which the spirochetes tend to accumulate in greatest numbers are the perivascular lymphatics.

These same conditions, Brown and Pearce point out, are equally true for the rabbit, and during active periods of infection spirochetes can always be recovered from superficial lymph nodes with greater ease and in greater number than from the blood; at times the nodes are almost as infectious as the active lesions. With the disappearance of lesions and of spirochetes from the blood, a condition develops in the

rabbit which may be regarded as true latency. During this period a slight adenopathy persists, and spirochetes can still be recovered for months or even years from the most easily accessible masses of lymphoid tissue.

The assumption seems warranted, therefore, that while the spirochetes are widely distributed over the body during latent as well as active periods of infection, the distribution is not an indiscriminate one but that the chief reservoirs of infection are the lymphoid structures of the body whether massed, as in the case of the lymph nodes, or in the form of the simpler perivascular lymphatics. This points to the possibility of a wide application of our knowledge of lymphoid involvement in diagnostic and prognostic measures.

STUDIES ON THE DISSEMINATION OF SPIROCHETA PALLIDA FROM THE PRIMARY FOCUS OF INFECTION IN RABBITS. In this investigation Brown and Pearce⁹² determined the infectivity of inguinal lymph nodes and the circulating blood of rabbits at various intervals after scrotal or testicular inoculation with syphilis. An emulsion was made of the lymph nodes and injected into normal rabbits. It was found, in a series of twenty-three animals, that the invasion of the lymph nodes by *Spirochetæ pallida* antedated both the appearance of the initial lesion and the occurrence of definite alteration in the nodes themselves, and that this occurred constantly within a period of less than forty-eight hours from the time of inoculation.

The blood was found to be infected with spirochetes one week after inoculation with syphilis.

In another experiment ten rabbits were inoculated in the right scrotum only, and forty-eight hours later the entire scrotum and testicle of this side were amputated. In spite of the complete removal of a wide zone of tissue surrounding the area of inoculation, all of these animals developed syphilitic lesions, this showing that true infection of parts outside of the zone of operation had taken place within the brief period of forty-eight hours.

This study of Brown and Pierce shows the futility of excising the chancre as a therapeutic procedure. It recalls the following recorded observation of Fournier: An individual after exposure to syphilis by sexual intercourse was circumcised forty-eight hours later. Although no chancre developed, yet secondary syphilis appeared within the prescribed time. Fournier, when commenting on this observation, stated that it was his belief that inoculation occurred on the foreskin and that the virus of syphilis rapidly leaves the area of inoculation. This observation was cited by those opposed to the practice of excising the chancre in the treatment of syphilis. It will be recalled that the justification of such a procedure was long a subject of debate by the earlier syphilologists.

IMMUNITY DEVELOPED BY THE REACTION TO SYPHILITIC INFECTION IN RABBITS. This study by Brown and Pierce⁹³ is of practical importance, inasmuch as it has a bearing on the early therapy of syphilis.

These investigators compared the results of unilateral to bilateral

⁹² Archives of Dermatology and Syphilis, October, 1920.

⁹³ Ibid., December, 1920.

inoculation in the scrotum and in the testicle, also unilateral and bilateral castration after inoculation, and suppression of the primary reaction by the use of therapeutic agents and complete prevention of a primary reaction.

Of 20 rabbits inoculated in both testicles, 14 were castrated and 6 held in control. Generalized lesions developed in one of the 6 controls and in 13 of the 14 castrated animals within the period of observation.

Twenty-seven rabbits were inoculated in one testicle only; 14 of these were castrated and 13 were held as controls. In the series, generalized lesions developed in 8 of the 13 controls as contrasted with 1 of 6 animals inoculated in both testicles and again in 13 of the 14 castrated animals. The results of these experiments demonstrate that, by inoculating one testicle instead of two, the incident of generalized lesions is greatly increased. When the reaction at the site of inoculation was further reduced by early removal of the infected organs, generalized lesions developed in almost every instance.

In a second set of experiments in which castrations were made at different stages of the infection, the effects of suppression of the testicular lesion by the use of a therapeutic agent was also tested.

Twelve rabbits, 6 of them inoculated unilaterally and 6 bilaterally, were given a single intravenous injection of arsenophenyl-glycyl-dichlorom-aminophenol (5 mg. per kilo) fourteen days after inoculation, and the results were compared to 6 untreated rabbits from each of the respective groups.

The result of this experiment showed that by properly gauging the dose of a therapeutic agent so as to suppress the lesions present without destroying the infecting organisms, the infection can be intensified in the same way as by an excision of the primary lesions.

From these experiments Brown and Pierce conclude that the reaction which takes place at the site of inoculation tends to dominate the entire course of the infection; that in effect this reaction either inhibits or obviates the necessity for the development of lesions elsewhere, and conversely, that the reduction or suppression of the reaction by the use of any means that does not exercise an equal effect on the organisms themselves removes this control and tends to increase the occurrence of generalized lesions and the severity of the infection.

From Bronfenbrenner and Schlesinger's⁹⁴ observations on experimental syphilis in rabbits, it was shown that under comparable conditions of infection untreated animals may thrive better than those receiving exceedingly small doses of the drug, although larger doses were remedial in the usual manner.

From a practical aspect, these observations are of importance. It emphasizes, what has been observed clinically, that the early insufficient treatment of syphilis with arsphenamin is potent of harm. The administration of one or two doses of arsphenamin in the early stage of syphilis, as the only means of treatment, is, in many cases, intimately associated with the subsequent development of neurorecidive. Indeed, early

⁹⁴ Proceedings of the Society of Experimental Biology and Medicine, December, 1920.

insufficient use of arsphenamin has been accused of causing the development of precocious syphilis and of early-appearing tertiary syphilis.

These observations recall the practice of the earlier syphilologist in awaiting the appearance of the secondary eruption before beginning treatment, not only to insure the diagnosis of syphilis, but in order not to disturb the orderly course of events.

Studies of Arsphenamin and Neoarsphenamin. The relative therapeutic value of arsphenamin and neoarsphenamin is discussed by Schamberg.⁹⁵ In addition to the simplicity of the technic of neoarsphenamin administration as contrasted with arsphenamin, there are more important questions which relate to the comparative curative properties and to the toxicity of the two compounds.

The reviewer thinks that most syphilographers believe that arsphenamin is more curative than neoarsphenamin, and in this they are correct. The circular accompanying the original German neosalvarsan marketed in this country stated, "The activity of neosalvarsan is at least as great as that of salvarsan." The reviewer believes this is erroneous.

According to the arsenic content of the two compounds (about 20 and 30 per cent respectively) 0.9 grain of neoarsphenamin should be equivalent to 0.6 grain of arsphenamin, but, as a matter of fact, it is not. In a paper recently read before the Pathological Society of Philadelphia, Schamberg, Kolmer and Raiziss showed that instead of requiring $33\frac{1}{3}$ per cent more neoarsphenamin than arsphenamin to sterilize rats experimentally infected with *Trypanosoma equiperdum* (horse syphilis or "la dourine") it required approximately twice as much of the former. This trypanosome reacts chemo-therapeutically much in the same manner as *Spirochetæ pallida*.

It might be admitted that twice as much neoarsphenamin as arsphenamin must be given to achieve the same results. In terms of arsenical content, one-third more arsenic would be introduced into the body. This would appear to be most undesirable were it not for other factors.

Schamberg, Kolmer, Raiziss and Weiss⁹⁶ demonstrated that arsphenamin, in practically all concentrations in which it is used, hemolyzes red blood cells *in vitro*. Neoarsphenamin, on the other hand, does not hemolyze the cells in any of the concentrations ordinarily employed. Furthermore, the hydrogen-ion concentration of neoarsphenamin is practically that of the blood, whereas both alkaline and acid solutions of arsphenamin are very different in hydrogen-ion concentration. There is therefore less biochemical disturbance of the blood and tissues after the administration of neoarsphenamin.

Studies of the comparative toxicity of arsphenamin and neoarsphenamin are most interesting. In general terms neoarsphenamin is over two and one-half times less toxic for white rats by intravenous injection than the arsphenamin from which it is made. A lot of arsphenamin which is tolerated by rats in the dose of 100 mg. per kilogram of body weight, when converted into the "neo" compound will be tolerated in from 250 to 300 mg.

⁹⁵ Journal of the American Medical Association, December, 1919.

⁹⁶ Archives of Dermatology and Syphilis, March, 1920.

The addition of the "formaldehyde sulphonylate group" apparently lessens the affinity of the compound for the protoplasm of the parasite, but seems to lessen the affinity for the body proteins still more. The lessened affinity is due to the closing of one of the "amino" groups.

We should expect, from the foregoing observations, that neoarsphenamin would be subjectively better tolerated than arsphenamin, and this, as a matter of fact, is the general experience. It must be realized that neo-arsphenamin is much more unstable and therefore undergoes change in the powder form much more readily than arsphenamin.

It should never be administered if the solution is not brilliantly clear, for a cloudy solution will produce immediate reactions, with syncope (in rare cases fatal) as the dominant symptom.

Some years ago Ehrlich announced that 0.9 gm. neosalvarsan possesses the curative value of 0.6 gm. salvarsan. Clinical observation, however, justified one in the belief that neoarsphenamin in the amounts commonly administered (0.6 to 0.9 gm.) does not appear to possess the same therapeutic activity as arsphenamin (0.4 to 0.6 gm.).

The work of Schamberg, Kolmer and Raiziss⁹⁷ has a distinct bearing on the comparative therapeutic activity of arsphenamin and neoarsphenamin. These workers made a comparative study of the trypanocidal activity of arsphenamin and neoarsphenamin. In this study, rats infected with a virulent strain of *Trypanosum equiperdum* were utilized in order to ascertain the smallest amounts of arsphenamin and neoarsphenamin produced by various laboratories that would sterilize animals injected twenty-four hours before the intraperitoneal injections of approximately known numbers of trypanosomes.

These experiments showed that with the strain of *Trypanosomes equiperdum* employed the smallest amounts of arsphenamin sterilizing rats infected twenty-four hours previously varied from 0.01 to 0.03 gm. per kilo of body weight, the general average for twenty-one compounds prepared by six different laboratories being 0.023 gm. per kilo of rat.

The smallest sterilizing doses of neoarsphenamin under identical conditions varied from 0.02 gm. to more than 0.04 gm. per kilo of rat; the general average for twenty-two compounds from six different laboratories was about 0.04 gm. per kilo.

The trypanocidal activity of different lots of arsphenamin and neoarsphenamin prepared by the same laboratory and by different laboratories varied in a manner analogous to variations in lethal toxicity for rats.

The trypanocidal activity of arsphenamin is 1.74 times greater than that of neoarsphenamin; in experimental infections with *S. obermayeri*, hen spirillosis and rabbit syphilis, Castelli found arsphenamin from 1.5 to 1.78 times more active therapeutically than neoarsphenamin.

According to these results, 0.6 gm. arsphenamin equals 1.05 rather than 0.9 gm. of neoarsphenamin in therapeutic activity.

The trypanocidal dose (*dois therapeutica*) of arsphenamin is 4.56 times less than the highest tolerated dose for the rat (*dois tolerata*);

⁹⁷ American Journal of the Medical Sciences, July, 1920.

the trypanocidal dose of neoarsphenamin is 6.35 times less than the highest tolerated dose.

These studies therefore indicate that neoarsphenamin is a somewhat safer compound than arsphenamin; even when 1 gm. of neoarsphenamin is administered as an equivalent in therapeutic activity to 0.6 gm. arsphenamin the margin of safety is greater.

In another communication⁹⁸ these workers report the results of a comparative study of the toxicity of arsphenamin and neoarsphenamin prepared by various laboratories. In this investigation rats were injected intravenously with solutions of the drugs.

In these tests animals showed "lethal toxicity" only, that is, the duration of life after the administration of given amounts per gram of body weight; they do not give rise to the transient untoward effects of arsphenamin and neoarsphenamin ascribed to faults of technic in the preparation and injection of the solution and the presence of an unidentified toxic substance designated as "X," which we believe may be present in the compounds themselves and produce the "nitritoid crisis."

The highest tolerated doses of arsphenamin and neoarsphenamin administered by intravenous injection to healthy rats are about 0.105 and 0.254 gm. per kilogram of body weight respectively; neoarsphenamin is therefore about 2.4 times less toxic than arsphenamin. Calculated upon the basis of 70 kilograms as the body weight of an average person, the highest tolerated dose of arsphenamin may be placed at 7.35 gm. and of neoarsphenamin at 17.5 gm., providing the tissues of persons are approximately of the same susceptibility; comparative tests among rabbits, rats and mice in which the same amounts of drugs were given per gram of body weight indicate, however, that the larger and heavier animals are more susceptible, and very probably human subjects cannot tolerate these substances in doses proportionate to body weight as established in animals.

By subcutaneous injection in mice, neoarsphenamin was found to be half as toxic as arsphenamin, but when administered subcutaneously to rats, neoarsphenamin was found twice as toxic as arsphenamin.

So far as the toxicity of arsphenamin and neoarsphenamin may be determined by intravenous injection of solutions in rats, the single dose of arsphenamin commonly administered (0.6 gm.) may be said to be about twelve times less than the highest tolerated dose and the highest single dose of neoarsphenamin commonly injected (0.9 gm.) is about nineteen times less; from the standpoint of margin of safety larger amounts of neoarsphenamin may be given and maintain the same ratio between *dosis therapeutica* and *dosis tolerata*, as apparently exists with arsphenamin.

ARSPHENAMIN AS A MEANS TO PREVENT INFECTION WITH SYPHILIS. In last year's review I wrote concerning the value of intravenous injections of arsphenamin to abort infection with syphilis in those exposed to the disease. Since this review other reports have appeared.

Golay⁹⁹ sums up the results of his observations in the use of such

⁹⁸ American Journal of the Medical Sciences, August, 1920.

⁹⁹ Ann. des mal. ven., November, 1920.

methods as follows: The use of the intravenous injections of arsphenamin as a prophylaxis in syphilis is indicated in all cases in which it is known positively that an individual has been exposed to syphilitic contagion. A prophylactic injection is also justified in all cases of chancre; also when it is known that a man has been exposed and is about to be married; and also if he has had extra-conjugal exposure. It should not be used, however, in cases of syphilophobia nor as a source of income. The dose should be not less than 0.3 gm. of neoarsphenamin and the size of the subsequent doses, probably six in all, would depend upon the tolerance of the patient. Golay has not been able to determine at what period of the incubation it ceases to become possible to sterilize the patient.

To my knowledge this has as yet not been determined. The use of arsphenamin in the above regard is spoken of as prophylaxis against syphilis; in reality, however, it is abortive treatment. We have no knowledge, either clinical or experimental, as to the value of arsphenamin when administered in a prophylactic manner.

Arsphenamin Icterus. Brodier¹⁰⁰ gives the results of his observations during the treatment of 636 syphilitics by neoarsenobenzol (Billon) injected intravenously in daily doses which did not in any case exceed 0.6 at one injection. The total amount of arsphenamin injected in the different patients varied from 3.5 gm. to 5.2 gm. Among the 636 syphilitics thus treated there were 39 cases of icterus, or a percentage of 6.77.

There are two types of icterus which occurred in this series of cases. The first type, which was by far the smaller in number developed during the course of the arsenical treatment. This type is spoken of as the "precocious icterus." The other type occurs at a later date. A number of syphilographers, among whom may be mentioned Milian, maintain that the precocious type of icterus is syphilitic in nature, and is, so to speak, a recurrence, whereas the late type of icterus is due to an intoxication by the arsphenamin. Other syphilographers maintain that either type may be looked upon as a catarrhal jaundice and may be induced directly or indirectly by the arsphenamin. Of the 38 cases of icterus studied, 11 were of the early and 27 of the late type.

Practically all of the precocious icterus cases developed the day following the injection. In 2 of the cases only it occurred the sixth and seventh days respectively after the injection. In the 2 cases the icterus was preceded by ordinary signs of gastro-intestinal disturbance on the day following the injection, and in one of these 2 cases marked signs of intolerance developed the day following the injection, consisting of fever and vomiting and gastro-intestinal disturbance. The patient had a marked intolerance for even very small doses.

The late type of icterus is much more common than the early type. There were 27 cases of this type. It most commonly developed in the first year of the infection, and, as a rule, between the sixth and twelfth months. The total amount of neoarsenobenzol injected before the onset

¹⁰⁰ Ann. des mal. ven., August, 1920.

of the late type of icterus varied from 3 gm. to 5.5 gm. There is a direct relation existing between the total amount of arsphenamin injected and the percentage of the cases of icterus. Approximately half of the late type of icterus cases were subsequently treated with arsphenamin without any untoward results.

The authors conclude from their studies that icterus may be, in certain cases, a hepatic recurrence, but that it does not seem to be directly the result of syphilis. They believe that arsphenamin in sufficient dosage favors indirectly the production of a toxic infectious icterus which is ordinarily benign in the patient predisposed toward jaundice. Secondary syphilis, particularly from the sixth to the twelfth months, often produces a parenchymatous hepatitis the modifications of which are the principal causes predisposing to this type of icterus.

They advise caution in regard to treating patients with arsphenamin during the period of the icterus, for the reason that it is possible that a benign icterus may be transformed thereby into a malignant icterus.

Another group of 55 cases of icterus observed in the course of one year which had developed during the treatment of 1100 cases of syphilis was reported by Clement-Simon and Vulliemoz.¹⁰¹ All the patients were ambulatory dispensary cases, and therefore some of the studies which would otherwise have been carried out were not made because of the inaccessibility of the patient.

The date of the appearance of the icterus varied within wide limits. In 32 cases the icterus was observed within one month after the last injection, and quite frequently it appeared during the course of the series. In a number of cases the patient who had received one series of injections without the development of icterus developed icterus during the course of the second series. In 22 cases icterus developed more than one month after the last injection. In 1 case the icterus developed thirteen months after the end of the medication. No relationship seemed to exist between the duration of the syphilitic infection and the development of icterus.

The duration of the icterus varied between three and five weeks. In all the cases it spontaneously disappeared. Most of the patients continued their occupations and did not even go on the milk and vegetable diet which was prescribed for them. The treatment was very simple and consisted of a calomel purgation. No arsenical treatment was given those patients who had had no active manifestations, but patients who did present active manifestations were given further arsenical medication during the attack of icterus, and these individuals made, likewise, uneventful recoveries.

The prognosis of arsphenamin icterus is excellent. No *icterus gravis* developed and no sign of sclerosis of the liver appeared. There appeared to be little, if any, relation existing between signs of intolerance and the development of icterus. Only in 11 cases had there been previous reaction, such as headaches, vomiting and fatigue.

¹⁰¹ Bull. Soc. franç. de dermat. et de syph., July, 1920.

Histological Changes Produced Experimentally in Rabbits by Arsphenamin, by Neoarsphenamin and by Mercurial Compounds. Kolmer and Lucke¹⁰² report, in a series of papers, their results of the above study.

The fatalities among persons following the administration of arsphenamin and neoarsphenamin in the treatment of syphilis have been mainly attributed to the toxicity of the drugs and to technical errors in administration referable to the preparation of the solution and manner of injection. The results of studies of the gross and histological tissue changes have usually shown the presence of some form of acute nephritis and degenerative changes in the liver as the most prominent lesions. In Europe an acute hemorrhage and "serous" meningitis, or, rather, an acute meningeal congestion, has been commonly described, whereas in America few or no changes in the membranes and substances of the brain and cord have been found. Under these circumstances, however, only limited information can be gained regarding the tissue changes ascribable to the solutions of the drugs because of pathological changes in the organs and tissues due to syphilis, for which the majority of persons succumbing after injections of arsphenamin have been treated.

A study of the effects of arsphenamin and neoarsphenamin on the tissues of experimental animals has proved of interest in two main directions, namely, as bearing on the methods of treatment of syphilis with these compounds and on the subject of specific arsenic therapy.

For example, in reference to the treatment of syphilis, differences in the degree of tissue changes, which were sometimes quite evident, have been found after the intravenous injection of arsphenamin and neoarsphenamin, and profound differences have been observed according to the kind of solution of arsphenamin administered, as acid and alkaline (disodium) solutions.

White rats and rabbits were employed in all experiments. Arsphenamin was administered by injection into the saphenous veins of rats; rabbits were injected with a syringe by way of the ear veins.

As a result of these studies, it was shown that the intravenous injection of lethal doses of acid non-neutralized solutions of arsphenamin in experimental animals produces widespread and severe vascular injury characterized by congestion, thrombus formation and hemorrhage; later, cellular degeneration and necrosis take place.

The intravenous injection of single large doses of solutions of disodium arsphenamin (ten times larger than the maximum amount administered to human beings at one time) produce severe vascular and tissue alterations, particularly in the liver, kidney, suprarenals and spleen. Similar, but less profound, changes were observed in the brain and meninges, heart and lungs.

The intravenous injections of multiple therapeutic doses of solutions of disodium arsphenamin corresponding to doses of 0.6 gm. per 60 kilos of body weight, produce inconspicuous tissue alterations that do not appear to be sufficiently pronounced to interfere with the functions of the organs.

¹⁰² Archives of Dermatology and Syphilis, Part II, April, 1921.

These changes were induced by arsphenamin prepared by several different laboratories and probably bear an important relation to arsphenamin reactions and to methods of arsphenamin therapy.

In the experiments with neoarsphenamin, it was shown that the intravenous injection of single massive and multiple smaller doses of neoarsphenamin into rats and rabbits produces vascular injury, cellular degenerations and necrosis similar to those produced by solutions of disodium arsphenamin. Histological changes were found in the cerebrum, cerebellum, brain-stem, meninges, heart, lungs, liver, kidneys, suprarenals and spleen. These changes are less severe than those produced by solutions of disodium arsphenamin when considered in relation to dosage per kilo of body weight.

The changes described were produced in equal degree and with equal frequency by neoarsphenamin prepared by different laboratories.

Neoarsphenamin in a single massive dose (0.200 gm. per kilo) produced somewhat less marked histological changes than single large doses of arsphenamin (0.100 gm. per kilo); likewise in smaller multiple doses neoarsphenamin (0.02 to 0.03 gm. per kilo) produced similar, but even less conspicuous, tissue injuries than arsphenamin (0.01 gm. per kilo).

It is to be emphasized that the histological changes produced by arsphenamin and neoarsphenamin were produced by relatively large doses of these drugs from three different manufacturers.

The results obtained from these studies should not create a false or unfavorable impression of the drug. The important practical deductions to be drawn from these studies, aside from their relation to the general subject of chemotherapy with arsenical compounds, are, that in relation to dosage, neoarsphenamin is less likely to produce tissue injury than arsphenamin, but that more information is desirable and necessary on the questions of dosage and elimination of both compounds, so that either may be employed in the treatment of disease with least possibility of producing injury.

From the standpoint of tissue injury alone, it would appear, therefore, that neoarsphenamin is somewhat more desirable for the treatment of syphilis than arsphenamin, but other factors are to be considered. This subject will be discussed later.

The experiments with mercury were made to study the histological changes produced in some of the internal organs of rabbits by different preparations of mercury administered by mouth and inunction and by intramuscular and intravenous injection as commonly employed in the treatment of syphilis. In the studies bearing on the histological changes produced in the rabbit by arsphenamin and neoarsphenamin, massive doses were administered to intensify the pathological changes in addition to multiple small doses, but in this investigation only small doses of the mercurials were administered comparable with the maximum therapeutic doses commonly employed in the treatment of syphilis.

It was shown that the administration to rabbits of different soluble and insoluble mercurial compounds commonly employed in the treatment of syphilis by intramuscular and intravenous injection, inunction

and oral administration, and in amounts analogous to the maximum doses given to human beings, resulted in the production of tissue changes in all organs examined, namely, the brain, heart, lungs, spleen, liver and kidneys.

The most conspicuous changes were found in the brain in the nature of perivascular round-cell infiltrations, and in the kidneys, as tubular and capsular glomerulo-nephroses of varying degrees of severity.

The degree of tissue injury caused by the different preparations of mercury appears to bear a direct relation to the actual amounts of pure mercury absorbed irrespective of the kind of preparation and route of administration.

Reactions after Arsphenamin and Neoarsphenamin. Numerous reports have appeared on the various reactions which from time to time follow the use of the arsphenamins. A large literature has already accumulated on this vexed subject.

Laboratory and clinical studies bearing on the causes of the reactions following intravenous injections of arsphenamin and neoarsphenamin have been reported by Schamberg, Kolmer, Raiziss and Weiss.¹⁰³ As a result of these studies it was concluded that the ingenious theory advanced by Danysz that intravascular precipitation of the organic arsenicals is the cause of the reactions (particularly the nitrotoxic reactions) after intravenous injection is only in part true. It explains the well-known precipitation of solution of acid arsphenamin and probably also concentrated solutions of monosodium arsphenamin (*i. e.*, arsphenamin neutralized to the point of clearing). There is no adequate evidence, however, that precipitation occurs after the use of disodium arsphenamin (hyperalkaline solutions), and there is no evidence at all that neoarsphenamin is ever precipitated in the blood.

The mechanism which Danysz sets forth as the cause of the precipitation, namely, conversion of the sodium salt of the drug into the insoluble base through the interaction of the sodium salt with the carbonates, phosphates and other inorganic salts of the blood, is not supported by experimental evidence. Experiments carried out by them indicate that the inorganic salts of the blood in the concentrations in which they normally occur do not precipitate alkaline solutions of arsphenamin and neoarsphenamin *in vitro*, either when tested alone or in the presence of the other organic or inorganic constituents of the blood.

Sodium bicarbonate alone forms a faint flocculation with minute amounts of disodium arsphenamin, but the precipitate dissolves readily on the addition of greater amounts of the latter. Acid arsphenamin precipitates readily in the presence of many of the inorganic salts of the blood; the precipitate, however, disappears when an excess of arsphenamin is added. Solutions containing even double the blood content of inorganic salts in an organic and protein menstruum ("artificial blood") do not form any appreciable precipitates with disodium arsphenamin *in vitro*. A faint flocculation which occurs occasionally with the first drop of arsphenamin, disappears when the second drop has been added.

¹⁰³ Archives of Dermatology and Syphilis, March, 1920.

Neoarsphenamin is not precipitated by any of the organic or inorganic salts of the blood. They believe that if arsphenamin is properly neutralized, that is, if the disodium and not the monosodium arsphenamin is injected, precipitation *in vitro* can scarcely take place.

The injections of acid solutions of arsphenamin are prone to produce death, or, if less concentrated, may lead to the development of a bronchopneumonia as a result of intravascular precipitation of the drug. Concentrated monosodium arsphenamin solutions may, under certain conditions, likewise cause death, or in the event of recovery cause an embolic bronchopneumonia. We have no knowledge that pneumonia symptoms have ever developed after the use of disodium arsphenamin nor after the use of neoarsphenamin.

The injection of cloudy or turbid solutions of neoarsphenamin will almost invariably give rise to severe nitritoid symptoms in which syncope and shock-like collapse are the outstanding features. No pulmonary symptoms follow. Neoarsphenamin (and, of course, arsphenamin) should never be administered unless the solution is perfectly clear.

Nitritoid reactions may at times follow the injection of a clear solution of neoarsphenamin. As neoarsphenamin is never precipitated in the blood, the elucidation of the cause of such reactions must be sought elsewhere.

The studies lead to a reiteration of the view previously expressed that the nitritoid reactions are related to some inherent property of the drug, probably traces of an unidentified impurity which is designated "substance X."

These studies are of practical importance inasmuch as they emphasize the vital importance of neutralizing arsphenamin, particularly if given in concentrated solutions.

On several occasions I have been consulted by physicians who inadvertently failed to neutralize arsphenamin before its administration. In these instances death followed the intravenous administration of a concentrated acid arsphenamin.

When preparing arsphenamin it is desirable to add a slight excess of alkali beyond the amount required to clear the solution—in other words, to administer the disodium salt rather than the monosodium salt.

The studies carried by Kolmer and Lucke indicate that the arsphenamins produce demonstrable effects chiefly on the liver, suprarenals and the bloodvessels, and mercury chiefly on the kidneys and brain. The arsphenamins would appear to have a special affinity for the organs referred to—a hepatotropism, an adrenotropism and a vasculotropism. Mercury possesses a nephrotropism, (an observation long known) and apparently a cerebrotropism, an observation which is, as far as we know, new.

Most of the fatalities following the use of the arsphenamins may be grouped under two heads—those referable to the liver and those affecting the brain and its membranes.

Kolmer and Lucke have shown that the arsphenamins in therapeutic dosage may induce slight structural changes in the liver and that huge

doses, such as are used to test the drug on animals, may cause quite considerable focal necroses. Warthin¹⁰⁴ says: "It is worthy of note that in a case of secondary syphilis dying of salvarsan-poisoning focal necroses containing spirochetes were present throughout the liver." In this connection the whole subject of jaundice in syphilis becomes pertinent for discussion. Without entering exhaustively into the subject, it may be said that there are several types of jaundice observed in syphilis: (a) True syphilitic jaundice, appearing before any treatment has been begun and due, doubtless, to a diffuse degeneration of the liver cells produced by *Spirochetæ pallida*; (b) jaundice due to the combined effect of hepatic syphilis and arsenical treatment (in these cases the jaundice is a sort of Herxheimer reaction); and (c) jaundice due to structural changes in the liver induced by the arsenicals and going on in some cases to the development of acute yellow atrophy.

It is a significant fact that jaundice is much more commonly observed in syphilis now than before the introduction of arsphenamin. Osler found jaundice in syphilis (before arsphenamin in 0.37 per cent of cases. Harrison¹⁰⁵ found jaundice in 0.6 per cent of cases of syphilis during or subsequent to arsenical treatment. Ravaut reports 20 cases of jaundice in patients receiving 94,672 injections of various arsphenamins. Scott and Pearson¹⁰⁶ observed 39 cases among 13,664 arsenical injections. Bailey and MacKay¹⁰⁷ studied 25 cases of toxic jaundice developing in patients receiving arsenical and mercurial treatment. Silbergleit and Fockler¹⁰⁸ report that they observed 13 cases of acute yellow atrophy of the liver, all fatal, and all occurring in syphilitic patients who shortly before had been given mercurial and neoarsphenamin treatment.

It can no longer be contested that jaundice and acute yellow atrophy are much more common nowadays than before the introduction of the arsphenamins. Nevertheless, we find a high incidence of such complications in certain countries and in the hands of certain clinicians and a low incidence elsewhere.

Is there any explanation for the discrepancy in the incidence of this complication? The writer believes that there is. In my own clinic in the Polyclinic Hospital (Graduate School of Medicine of the University of Pennsylvania) over 12,000 injections of the arsphenamins have been given, and we have only observed 3 cases of jaundice.

Furthermore, we have only encountered 2 mild cases of exfoliative dermatitis, a condition which is essentially an expression of arsenical intoxication.

What is the explanation of this low incidence of jaundice and exfoliative dermatitis? I believe it to be due to the fact that, for purposes of scientific investigation, our treatment of syphilis is an exclusive arsenical treatment. We are studying the effect of arsphenamin and neoarsphenamin on syphilis, and we do not complicate this study by administering

¹⁰⁴ American Journal of Syphilis, July, 1918, ii, 445.

¹⁰⁵ Quarterly Journal of Medicine, July, 1917, xl, 321.

¹⁰⁶ American Journal of Syphilis, October, 1919, iii, 629.

¹⁰⁷ Toxic Jaundice in Patients under Antisyphilitic Treatment, Archives of Internal Medicine, June, 1920, xxv, 6286.

¹⁰⁸ Ztschr. f. klin. Med., 1919, lxxxviii, 333.

mercury. The arsenical treatment is fairly vigorous, patients receiving two 0.4 gm. doses of arspenamin or two 0.9 gm. of neoarsphenamin twice a week. Some patients have had this treatment continued until fifteen to twenty treatments have been given without interruption. We have never encountered a case of yellow atrophy of the liver or of encephalitis. In my private practice treatment has at times been much more intensive than that indicated above, and yet no hepatic, cerebral or cutaneous complications have occurred. I am of the opinion that conjoint mercurial and arspenamin treatment, while perhaps more curative, is more liable to complications and fatalities. Some clinics, in which mercury and arspenamin are conjointly used, encounter jaundice and dermatitis far more commonly than we do.

Wechselmann¹⁰⁹ says: "My entire experience with more than 25,000 injections forces me to conclude that salvarsan is much less toxic than mercury. My department, in which salvarsan is used almost exclusively, has given me much less care and trouble during the past three years than in the previous period when mercury was employed."

A remarkable and unfortunate series of cases of "Delayed Arsenical Poisoning" is reported by Strathy, Smith and Hannah.¹¹⁰ They describe 58 cases of late arsenical poisoning, 8 of which were fatal, the symptoms developing, on an average, forty-three days after the last arsenical treatment. Jaundice was the most prominent symptom, being present in all of the fatal cases and in 39 of the non-fatal group. There were also 8 cases of exfoliative dermatitis. The writers state that "intensive treatment" was used, *i. e.*, doses of arspenamin and mercury, each once a week for seven or eight weeks. Intramuscular injections of mercurial oil (gray oil) were given at the same time as the arsenical treatment. Nearly all of the patients were treated with foreign makes of neoarsphenamin. The patients were all between twenty and forty years of age. Necropsy examinations in most of the cases exhibited changes in the kidneys in addition to hepatic atrophy. The greatest total amount of arspenamin used in any case was less than 7 gm. and the least amount 2.2 gm. These cases in all probability represent arsenical poisoning due to the vigorous conjoint use of mercury and arsenic. The authors themselves suspected this, for they say: "A few of the patients showed slight symptoms of mercurial poisoning, but mercury is known to be an irritant of the kidneys and in excessive doses to cause degeneration of the tubular epithelium, and it seems not at all unlikely that for this reason it acted as a predisposing factor."

The pathogeny of such poisonings is reasonably clear. Mercury in vigorous dosage, particularly when the insoluble salts are used, may severely irritate the kidneys and inhibit their power to eliminate arspenamin. Within a short time after an injection of arspenamin, most of it disappears from the blood and is lodged in the organs, one of the chief reservoirs being the liver. If the eliminatory activity of the kidneys is impaired, it is obvious that the arspenamine will remain for a longer time and in larger quantities in the liver, for which organ it has a con-

¹⁰⁹ The Pathogenesis of Salvarsan Fatalities, trans., 1913, St. Louis, p. 106.

¹¹⁰ Lancet, April 10, 1920, pp. 802-807.

siderable affinity. Too long a residence in the liver may cause the drug either to become oxidized, with the production of arsenoxid, or the arsenical radical may become split off and produce the symptoms of arsenical poisoning.

The Salvarsan Committee,¹¹¹ appointed by the British Medical Research Council, in its first report referred to some outbreaks of toxic jaundice, attended by a high fatality, which occurred in certain military hospitals after the use of the organic arsenicals. At the suggestion of the committee, Dr. H. M. Turnbull¹¹² made an examination of the tissues from 8 fatal cases. He concludes that "The liver in all cases was the site of a severe pathological lesion, a lesion more severe than that in any other organs. . . . The liver was the seat of severe degeneration and necrosis.

"The kidney was available for examination in 6 cases, and in all showed a severe parenchymatous degeneration." No true nephritis was present. Turnbull regarded the kidney changes as secondary.

Comparative Effect of Arsphenamin and Neoarsphenamin. While the studies of Kolmer and Lucke indicate that similar structural changes occur after the use of arsphenamin and neoarsphenamin, they call attention to the fact that the changes are distinctly less severe after neoarsphenamin. This finding is in harmony with clinical observation. It may be definitely stated that neoarsphenamin has less than one-half the toxicity of arsphenamin and is unquestionably a safer remedy. This is due in part to the fact that one of the anchoring groups—amino group—is closed, and, furthermore, to the fact that neoarsphenamin is neutral in reaction and does not in ordinary concentration produce hemolysis.

Structural Changes Induced by Mercury. It has long been known that mercury has an affinity for the kidneys and that mercurial-poisoning is apt to be associated with a nephritis. Accidental poisoning with mercuric chloride kills in this manner.

The studies of Kolmer and Lucke are interesting in that they demonstrate that relatively short courses of mercury may produce perceptible renal changes. Even in rats that received treatment by mouth for from four to six weeks, recognizable changes were observed in certain organs. These rats received 2 mg. ($\frac{1}{30}$ grain) of yellow mercurous iodide a day. This would correspond to 2 grains daily for a man weighing 130 pounds. This is somewhat larger than the ordinary therapeutic dose but not greater than the old method of administering an increasing number of pills daily until "some characteristic toxic effect of the drug is produced."

The pathological findings and clinical experience would alike persuade one to utter two cautions: In mercurial treatment, watch the kidneys; in arsphenamin treatment, watch the liver. To be sure, as stated by Milian, in early syphilis jaundice may indicate either hepatic syphilis or a Herxheimer reaction, and will respond to more vigorous treatment when the less intense treatment has failed. Later in the disease, however,

¹¹¹ Privy Council, British Medical Research Council, Special Report, 1920, Series 44

¹¹² Privy Council, British Medical Research Council, Special Report, 1920, Series 55.

and particularly after the vigorous use of the arsenicals, the development of jaundice should lead to a suspension of all specific treatment. The treatment of syphilis requires the repeated use of these drugs. When used with circumspection and good judgment, harmful results may in large part be avoided. When used unskillfully, without proper examinations of the patient and without knowledge of warning signals, unfortunate results may take place. The fact should be emphasized that the body tolerates much larger amounts of arsphenamin than mercury. The therapeutic dose of arsphenamin is infinitely more destructive to the spirochete of syphilis than the therapeutic dose of mercury. Fatalities have occurred both after arsphenamin and mercury. Those after the former are much more tragic and fear-inspiring, for the relation between cause and effect is obvious. Many scores, if not hundreds, of deaths after mercury have likewise been reported in the literature, but they are ordinarily more apt to be slow and insidious, and less likely to be incriminative of the therapeutic procedure employed.

In conclusion, it may be said that vigorous mercurial treatment is often responsible for arsenical intoxication when arsphenamin and mercury are used at the same time. Large doses of both ought not to be employed synchronously. When the two are used jointly, their respective dosages should be inversely proportional to each other. It would appear best to give the courses of mercury subsequent to that of arsenic.

DISEASES OF THE NERVOUS SYSTEM.

BY WILLIAM G. SPILLER, M.D.

Epidemic Encephalitis. Pierre Marie and Gabrielle Lévy¹ have made an interesting study of the involuntary movements in this disease. They state the excito-motor syndrome may appear in four forms: As an early and fleeting manifestation of the infection; as an early and prolonged manifestation; as one appearing a week after the first signs of the disease; and as a tardy manifestation, two or three months, sometimes six months, after the onset of the disease. It may be the essential or exclusive sign of the disease. The Parkinson syndrome they have found appears a few days or a week, sometimes two or three weeks, after the onset of the disease. The diffuse chorea appears to lessen or disappear after some months, some other forms last a year and a half, but these observers are unable to make any statement regarding the duration of the Parkinson type.

A very important study of epidemic encephalitis has been made by Mingazzini² from more than 100 cases. It is not possible to refer in detail to this paper here, but one or two disputed questions may be considered. He finds that the paralysis agitans precox postencephalitica develops with the same symptoms as does the ordinary paralysis agitans. Souques and de Massari believe it is a true form of paralysis agitans, not a mere resemblance in symptomatology, but Mingazzini shares the view of Sicard and Paraf in accepting in addition to a true Parkinsonian form another form, almost always curable, characterized by the typical rigor and tremor of the hands, or by hypertonia and rigidity of expression. There seems to be no way in the beginning of this symptom complex to determine in a given case whether there is to be cure or not, but it is most encouraging to know the Parkinson form is not always persistent.

He has found serious invasion of the spinal cord, and he gives two pictures representing a considerable cellular infiltration of the spinal pia and nerve roots. In 1 case he found small scattered hemorrhages in the substance of the cord with cellular infiltration, but in addition he also found plasma cells and lymphocytes between the bundles of the anterior roots. The radicular form of epidemic encephalitis has been based chiefly on the clinical findings.

Sicard and Paraf³ were able to present at a meeting 5 cases of paralysis agitans resulting from epidemic encephalitis. The cases of the myoclonic form of epidemic encephalitis seem to be becoming very numerous. At another meeting of the Society of Neurology of Paris the subject of

¹ *Revue Neurologique*, June, 1920, p. 513.

² *Zeitschrift für die gesamte Neurologie und Psychiatrie*, lxxiii, 199.

³ *Revue Neurologique*, 1920, No. 5, p. 463 and No. 6, p. 562.

the paralysis agitans complex resulting from lethargic encephalitis was considered again and several cases were presented.

Souques had seen 4 or 5 cases of the Parkinson type, in 1920 and he refers to the fact that infection has been regarded as the cause of Parkinson's disease, especially by Gowers and Dana, and he believes the infection may be from typhoid fever, pneumonia, scarlet fever, etc., but other cases may be from intoxication, auto-intoxication, and arteriosclerosis. He does not believe, as some have, that severe emotion alone may be a cause.

Since his previous report, Souques⁴ has observed 10 more cases of the form of encephalitis resembling Parkinson's disease, making a dozen cases in all. The Parkinsonian form is most likely to be in children, probably because lethargic encephalitis has been found to occur more frequently in children. The Parkinsonian form appeared in 7 of Souques' cases during the initial phase of the encephalitis, but in 3 cases it did not appear for several months after the onset of the encephalitis. Two of these cases seemed to be with recovery, but later the symptoms of Parkinson's disease reappeared. This does not mean that permanent recovery is impossible, as Sicard has reported cases with recovery, although Souques has not observed this happy result. Six of his cases were progressive, and in 1 case the symptoms had persisted for three years.

Souques observed, in 2 of his cases, phenomena not pertaining to the ordinary form of paralysis agitans, such as choroid-athetoid movements or spasms of the face, and the explanation probably is found in the extent of the lesions in encephalitis.

TREATMENT OF POSTENCEPHALITIC PARKINSON SYNDROME. Rodriguez,⁵ of Barcelona, reports his experience with the use of cacodylate of soda in treating the rigidity resembling that of Parkinson's disease following epidemic encephalitis. This treatment has been employed by others also for Parkinson's disease occurring independently of encephalitis, and for spastic conditions of different types, and apparently with success. The intravenous route has been preferred.

Rodriguez states that the intravenous administration avoids local disturbance such as aseptic abscess, and is more rapid and definite in its effects. The intramuscular injections are painful and less active in equal doses with the intravenous injections. He employs fourteen or fifteen injections to a series, with large doses, and three or four series in the treatment; for the doses it seems wiser to refer to his paper. It is not well to stop the arsenic suddenly, as mental and physical depression, temporary increase of spasticity, etc. may result from sudden discontinuance of the arsenic. Accidents have been rare, but twice he has seen gastro-intestinal signs of intoxication; nausea, vomiting and diarrhea; also twice he has observed chills, increased frequency of pulse without fever; and sometimes headache has resulted, but never symptoms of neuritis. This last statement is very important because one would fear arsenical neuritis after large doses given over a long period. The therapeutic effects are these:

⁴ *Revue Neurologique*, 1921, No. 2, p. 178.

⁵ *Ibid.*, No. 1, p. 111.

The subjective and objective sensation of rigidity of the limbs and of the neck diminishes greatly or even disappears, the motor agility increases, there is less bending forward and better gait. The great muscular hypertonia is replaced by slight hypertonia or even hypotonia, the tendon reflexes become normal but never disappear, the paralysis of accommodation becomes less, the mental condition is one of greater activity and less fatigue follows effort, lethargy disappears and sleep becomes normal, appetite and body weight increase, the mental condition improves greatly. All this seems a very remarkable accomplishment.

MYOCLONIC FORM OF EPIDEMIC ENCEPHALITIS. A number of observers have described the myoclonic movements of this disease. Piero Boveri⁶ studied them in Milan, and described 2 cases in which the striking symptoms were myoclonic convulsions, both rhythmic and partial, as though produced by an electric current, and he refers to the description given by Dubini in 1846 and not mentioned since his time.

J. Ramsay Hunt⁷ describes the disorder as having an acute onset characterized by sharp shooting pains in the trunk and limbs, at first local but rapidly becoming generalized. They may reach an extreme degree of intensity. The pains are soon followed by muscle jerks, waves and twitchings, in the painful regions. The twitchings are bilateral and multiple, and may be generalized. A tendency to localization in certain regions of the body may occur, the muscles of the abdomen and lower extremities showing an especial vulnerability. The contractions are of quick clonic character, involving individual muscles or portions of muscles, but not synergic groups, so that the resulting locomotor effect is comparatively slight.

There is sometimes well-marked delirium, which varies in duration and intensity with the severity of the infection. In milder types there may be only irritability, restlessness and insomnia, associated with anxiety and apprehension. The myoclonus delirium presents the characteristics of a toxic delirium, and is characterized by hallucinations, illusions and transitory delusions. There are restlessness, insomnia, apprehension, disconnected thought and mental confusion. The symptoms are more conspicuous at night.

Moderate fever may occur during the course of the disease, with acceleration of the pulse, and often hyperhidrosis. There is no tenderness of nerve trunks, and no paralysis of any muscle or group of muscles. The sensory disturbances are pain, hyperesthesia and occasionally paresthesia in the distal parts of the limbs.

Hunt acknowledges the relationship of this myoclonic form to epidemic encephalitis, as shown not only by its prevalence at the same time, but also by various combination forms (cranial nerve palsies and myoclonus) which have been encountered. There is quite a question whether much is gained by separating the myoclonic form. A few quick jerking movements in a limited area is not a rare occurrence in any case of lethargic encephalitis.

⁶ Journal of Nervous and Mental Disease, May, 1920, p. 409.

⁷ Journal of the American Medical Association, September 11, 1920, p. 713.

Still another type has been separated by Pardee,⁸ which he designates as acute descending radiculitis. He has observed the cases during the influenza epidemic. Radiating pain is first felt in the upper chest, then girdle sensations are felt around the waist. While the symptoms are at their height in the intercostal and abdominal regions there is delirium, but the pain is usually less severe. The symptoms then affect the legs, the pain increases greatly in intensity. A slight increase in fever precedes the invasion in the lumbo-sacral region, which diminishes again in about four or five days. Thereafter a slow convalescence of many weeks' duration begins. During this convalescence there is a coarse tremor of the arms and legs.

There is much in this description to suggest the myoclonic form. Abrahamson, in discussing this paper, regarded it as a mistake to speak of a spinal type of encephalitis. To pick out a part of the clinical picture and to label it a type is not sound teaching. All types of radiculitis are to be found, local, unilateral, ascending, descending, migrating; occasionally or for a time its signs dominate the clinical picture, more frequently it is secondary to other signs and symptoms. He has found radicular signs in at least 60 per cent of the cases of encephalitis. The most common sites are the cervical cord, next the midthoracic, and next the lower lumbar region.

Walshe⁹ has stated that the numerous schemes of classification of epidemic encephalitis, though inevitable in the early and growing stage of knowledge of so polymorphic a disease, are in fact tending to confuse rather than to lend precision to our conceptions of this malady, for practically every case presents, either simultaneously or at some phase of its course, the features of several clinical types. Myoclonic encephalitis has been applied to different forms of movements, and myoclonic movements are a common manifestation of different forms of the disease. He suggests a classification on an anatomical basis, but this has difficulties. He shows that where the virus produces negative or paralytic symptoms it has, ever since the first appearance of the disease, shown a definitive and characteristic selective action on the cells of the basal ganglia and on those of certain motor nerves in the brainstem, producing the familiar basal ganglia and midbrain types of the disease with its associated lethargy. On the other hand, in its irritative or exciting effect the virus appears to act equally on any and every part of the nervous system, from cerebral hemispheres to spinal roots, hence the polymorphic character of cases showing irritative symptoms. It is such cases that present the many difficulties in any attempt to classify lethargic encephalitis into clinical types. Possibly, he thinks, we may be dealing with a complex virus in which more than one active component exists.

INSOMNIA IN EPIDEMIC ENCEPHALITIS. Lethargy not only may be absent in this disease but, as Happ and Blackfan¹⁰ have shown, insomnia may be a striking symptom. These authors have observed a number of

⁸ *Journal of Nervous and Mental Disease*, May, 1920, p. 456.

⁹ *Brain*, vol. xliii, part III, p. 197.

¹⁰ *Journal of the American Medical Association*, November 13, 1920, p. 1337.

children who were brought to the hospital because of inability to sleep at night. From their observation of these cases they are convinced that persistent insomnia is a fairly common sequel of acute epidemic encephalitis in children. Their first case puzzled them as to the nature of the condition. The nightly repetition of sleeplessness and excitability, followed by deep sleep in the daytime, suggested the possibility that it was the result of encephalitis; but in the absence of a definite history of an acute illness, with fever, ocular paralysis, lethargy, etc., they were unable to substantiate the diagnosis. Subsequently they had the opportunity to observe five children with insomnia following encephalitis, and the striking similarity of the latter cases to the foregoing would seem to verify the diagnosis.

The duration of the insomnia in the first patient had been more than seven months, in the second, five months; in the third, four months; and in their last three patients six months each. Insomnia following acute disease, such as typhoid fever, they believe never lasts so long. The sleep of the neurotic child may be broken and irregular and it is frequently disturbed by dreams and night terrors, but the neurotic child does not have the deep, undisturbed early morning sleep. His sleep is usually light, and the slightest noise serves to awaken him. Several of their patients early in the disease had been regarded as having chorea because of the choreiform movements observed in this stage. These movements had not persisted and the disease had presented no close resemblance to true chorea.

Happ and Blackfan state that it is well recognized that there are cases of epidemic encephalitis which do not show the symptomatology of an acute febrile onset, ocular paralysis and pronounced lethargy, and there are well authenticated cases in which the paralyses may be entirely absent and lethargy may not appear. On the contrary, delirium, excitability and choreiform movements may be the predominant symptoms. They believe that nocturnal wakefulness, excitability and restlessness, followed by deep sleep, almost stupor, during the morning, accompanied by a change of disposition and behavior during the waking period, persisting for several months, is a characteristic syndrome following acute epidemic encephalitis in childhood. They rightly say that the term "lethargic" is unfortunate for several reasons, one of which is that it tends to induce the overlooking of non-lethargic cases. It is important that this condition be recognized in order that the children may be regarded as sick children and that the parents may be assured that the insomnia and other peculiarities are not caused by wilfulness and disobedience on the part of the child. The patients should be placed in a quiet environment, permitted to sleep when they choose, and not awakened in the morning for meals and bath. They should be given their noon meal and their evening meal, and a third meal should be given at night. They require careful attention at night, and must be prevented from harming themselves. Sedatives, as a rule, are not necessary and are not satisfactory. A definite statement as to the prognosis cannot be made, but there is no tendency to rapid improvement.

Crookshank¹¹ writes a letter in which he points out that we are in the ludicrous position of being assured regarding that epidemic encephalitis polioencephalitis, and influenzal encephalitis, each is distinguishable from the others by a pathological criterion which is sometimes present in all. On the clinical side, almost any combination of nervous symptoms may be produced, and he states Netter now admits that there is a poliomyelitic form of encephalitis and an encephalitic form of poliomyelitis. The alleged epidemiological differentiae are even less substantial, and Crookshank shows that the period of the year for the occurrence of these diseases is unreliable as a diagnostic feature. He says that not one single specific clinical, experimental, pathological, or epidemiological criterion can now be alleged in distinction between so-called encephalitis lethargica and poliomyelitis, polioencephalitis, or any other of these many forms of encephalitis, myelitis and neuritis that are epidemic during influenza periods.

For this reason what is known as the unitarian concept of epidemic encephalitis is gaining ground constantly outside of England, but it does not seem to have found much favor with English investigators. Crookshank seems to stand rather apart from his colleagues in this attitude he takes toward these diseases, as the tendency of most investigators has been to regard them as sharply differentiated disorders.

RECURRENCE OF SYMPTOMS is known in epidemic encephalitis. Sicard and Kudelski¹² had a patient, a girl of twenty years, who had diplopia and somnolence about two weeks, which then disappeared and she was able to resume her daily occupation. After two weeks of apparent recovery, diplopia and somnolence reappeared and were associated with facial palsy and hemiparesis, at first on the left side of the face and right side of the body, and later on the right side of the face and left side of the body.

These writers describe the myoclonic form as associated with pain and without somnolence.

Dufour,¹³ in January, 1920, spoke of an epidemic of hiccough he had observed and believed to be a form of lethargic encephalitis. Pain, fever and malaise were associated with the hiccough. He believed the phrenic nerve was affected, and he thought the disorder was usually benign, the hiccough lasting from one to four days and disappearing spontaneously. Later in the year numerous writers have described this epidemic hiccough.

Sicard¹⁴ has stated he believed the only symptom of epidemic encephalitis might be severe pain. He observed intense cervico-brachial pain, preventing sleep, with disturbance of sensation in the hand. Netter also has observed this form.

Sicard¹⁵ also describes a form of the disease with paralysis of the lower limbs. Netter¹⁶ states that the lesions of epidemic encephalitis may be pronounced in the spinal cord, and may be without the characteristic

¹¹ British Medical Journal, December 11, 1920, p. 916.

¹² Bulletins et Mémoires de la Société Médicale des Hôpitaux, 36th Year, 1920, p. 93.

¹³ Ibid., p. 263.

¹⁴ Ibid., p. 294.

¹⁵ Ibid., p. 306.

¹⁶ Ibid., p. 561.

lesions of the brain, or at least without symptoms of such lesions. He has seen three children and one adult with paraplegia or quadriplegia. There is therefore a poliomyelitis form of epidemic encephalitis just as there is an encephalic form of poliomyelitis. This necessarily complicates the diagnosis.

There is no doubt that this disease is communicable in some way but it is very unusual for more than one member of a family to contract it. Lévy¹⁷ has seen three children in one family with this disease, and in each case the type of the disease was different.

Netter gives some interesting information as regards the degree of contagion of epidemic encephalitis. He believes it is certainly contagious and probably through the saliva. The patient is capable of transmitting the disease during a very long period, and convalescents may convey the disease. The contagion may come from a patient with an abortive form or from a healthy person having been with a patient. He therefore advises that the family of a patient should be informed of the possibility of contagion, but he does not advise isolation because it is impossible to fix any period for this, and it is very seldom that transmission can be observed, although there are some cases which show this possibility. In a case reported by Tissier¹⁸ the contagion in a family seems to have occurred after eighteen months. Netter has observed 174 cases of epidemic encephalitis, of these a history of contact with the disease was obtained only in 8; three times two members of a family were affected, and two children with the disease were in an institution. The contagiousness resembles that of epidemic cerebrospinal meningitis.

Sicard and Comby,¹⁹ on the other hand, stated they had never seen a case of this disease which they could trace to another case, Sicard would recommend isolation if it could be done effectively, but he adds that for eighteen months he has had constantly in his hospital service cases of epidemic encephalitis and has never observed transmission of the disease to another.

This whole volume is so full of interesting clinical and some pathological reports on epidemic encephalitis that it has only been possible for me to select a few of the most interesting.

An interesting study of epidemic encephalitis based on 20 cases studied by the authors is given by Miner and Freeman.²⁰ The symptoms are discussed separately, but it would occupy too much space to give this discussion in detail here. The conclusion is one that can readily be accepted. They state that in any case presenting fever, cranial nerve paralysis, particularly of the third and seventh nerves, accompanied by stupor or lethargy, with muscular fibrillation and tremor, together with mask-like face, a diagnosis of epidemic encephalitis should be seriously considered. The spinal fluid was practically normal in all their cases, but they advise that spinal puncture should be made, when possible, to exclude cerebrospinal and tuberculous meningitis, anterior poliomyelitis

¹⁷ *Bulletins et Mémoires de la Société Médicale des Hôpitaux*, 36th Year, 1920, p. 1007.

¹⁸ *Ibid.*, p. 1030.

¹⁹ *Ibid.*, p. 1630.

²⁰ *American Journal of the Medical Sciences*, January, 1921, p. 91.

and cerebrospinal syphilis. There are many other conditions that may be confused with this disease, but they feel that cases of acute encephalitis are so characteristic and have so uniformly the same symptom-complex that the diagnosis can easily be made by one who has once seen the disease. One of their cases was complicated by gangrene, a very unusual disorder in this disease.

Davis and Kraus²¹ have observed the frequency with which variations have occurred in the colloidal gold test in epidemic encephalitis. These variations suggested syphilis, although there were no other serological (Wassermann) or clinical evidences of this disease. Abnormal colloidal gold reactions are evidence of pathologic changes, they believe, and are not of specific etiology.

ETIOLOGY OF EPIDEMIC ENCEPHALITIS. The work of Leowe and Strauss has received striking confirmation from Thalhimer. He believes there has been demonstrated an infectious agent which is apparently constantly associated with epidemic encephalitis. His results are identical with those that have been reported by Leowe and Strauss. They are confirmatory of both their animal experiments and cultural studies.

The infectious agent passes through a clay filter capable of holding back ordinary bacteria, and the filtrate produces a disease in rabbits very similar in its clinical features to those of the human disease. The microscopic brain lesions are identical with those found in fatal human cases.

The extremely minute filtrable microörganism, that has been successfully cultivated on ascitic fluid tissue medium from brain material and spinal fluid obtained from patients with epidemic encephalitis, is believed to be identical with the microörganism that has been cultivated by Leowe and Strauss.

The investigations of these men, followed by those of Levaditi and Harvier and of McIntosh and Turnbull, taken together with those reported by Thalhimer,²² strongly indicate that epidemic encephalitis is caused by a filtrable virus. The filtrable microörganism is believed to be the etiologic agent of epidemic encephalitis.

MENTAL DISTURBANCE IN CHILDREN IN EPIDEMIC ENCEPHALITIS. Leahy and Sands²³ state that for six months they have had occasion to study a group of children who had had epidemic encephalitis and who had subsequently shown sufficient mental disorder to warrant their family physicians sending them for observation to the psychopathic wards of Bellevue Hospital. These patients all had definite attacks of the disease, and they all showed a more or less uniform mental disorder after their apparent recovery from the acute phase of their illness.

Their ages varied from five to fourteen and a half years, and there were 4 boys and 2 girls. Their physical condition was such as to lead one to believe that there was no further action of the infectious agent, and that the disease process had come to a standstill. Their

²¹ American Journal of the Medical Sciences, January, 1921, p. 109.

²² Archives of Neurology and Psychiatry, vol. v, No. 2, p. 113.

²³ Journal of the American Medical Association, February 5, 1921, p. 373.

temperature, pulse, respiration, blood pictures and urine examinations were all normal. The Wassermann reaction in each case was negative.

Their mental status was characterized by purposeless, impulsive motor acts, marked irritability, definite attention disorders, distractibility and changing, variable mood, inadequate and inconsistent emotional reactions, marked insomnia and, in 2 cases, precocious sexual feelings and intense eroticisms.

Double Athetosis. There are many disorders attributed to disease of the lenticular nucleus and I²⁴ have grouped these in a recent paper. The pathology of these different diseases is obscure because no one knows why so many types result from lesions of the same part. The pathology of athetosis is made better known by a case studied by me. The patient, a woman, had been in the hospital thirty-seven years and presented during this long period marked spasticity, athetosis and contractures. The microscopical study showed that the putamen of each lenticular nucleus was intensely degenerated and proved that disease of these structures could cause athetosis.

Puncture of Cisterna Magna. This procedure is certainly radical, is it justifiable? As Ayer²⁵ says, the necessity of reaching the subarachnoid space at other points than the lumbar sac has led to such procedures as puncture in the thoracic and cervical regions, puncture through the sphenoidal fissure and intraventricular puncture, but no one before Ayer has used the cisterna puncture as a clinical procedure, although it has been the routine method for obtaining cerebrospinal fluid in animals. He believes the cisterna puncture renders access to a point of even more strategic value than thoracic, cervical or sphenoidal puncture, and should in some cases render intraventricular puncture unnecessary.

After describing the technic of the method, he states the discomfort to the patient is usually the same or less than in lumbar puncture. Twice only did he cause sudden transient pain on piercing the dura. Failure to reach the cisterna was experienced on two occasions, once in a patient with the neck greatly retracted from acute meningitis; and once it was deemed wise to desist on obtaining no fluid at the depth of 6 cm. The after-effects of cisterna puncture have been of no consequence, even when serum has been introduced. Whether puncture headache will follow this technic is not known, as the cases in which it was carried out were for the most part those in which headache does not occur from lumbar puncture.

The technic, Ayer thinks, should not prove difficult to one familiar with lumbar puncture, especially after preliminary practice on the cadaver. He has recommended the method (1) in spinal subarachnoid block following meningitis; (2) combined with lumbar puncture for irrigation of the subarachnoid space, and (3) as a route for serum injection in epidemic meningitis. He has performed cisterna puncture in 20 cases, all of which were examples of the first or third groups, but he has not had opportunity for irrigation. In all he has performed the puncture forty-three times; for diagnosis or treatment of postmeningitic

²⁴ Archives of Neurology and Psychiatry, 1920, No. 4, iv, 370.

²⁵ Ibid., vol. iv, No. 5, p. 529, and No. 4, p. 465.

block in 5 cases; for treatment in epidemic meningitis in 1 case; for diagnosis and treatment of cerebral syphilis in 5 cases, and for diagnosis of cord compression in 9 cases.

Cistern and lumbar fluids are practically identical so far as protein (quantitatively determined by colorimetric method), sugar (qualitatively estimated), cells, and colloidal-gold reactions are concerned. The pressures, as registered in two manometers simultaneously, are the same. In one case Ayer was able to demonstrate persistent pus in the spinal meninges, the basal cerebral membranes being presumably free from infection; in another to demonstrate persistent acute staphylococcus meningitis in the cerebral meninges with spinal meningeal block, and to treat successfully the cerebral infection by way of the cisterna magna.

As might be expected, this paper called forth much discussion when it was read before the American Neurological Association. Ernest Sachs said he would fear greatly to undertake such a puncture, and others recognized that the method is dangerous and not to be undertaken by a surgeon unless he has experimented on the cadaver. The method is one that must be tried with great caution and only by those familiar with spinal technic.

Multiple Brain Abscesses Secondary to Bronchiectasis. Saelhof²⁶ believes that in 60 per cent of cases of brain abscess the cause is a suppurative condition of the middle ear. Carious processes of the bones of the skull, chiefly the ethmoid, sphenoid, mastoid and frontal give rise to about 15 per cent. Orbital injury, nasal and pharyngeal infections, traumatism, foreign bodies, etc. cause approximately 15 per cent. Abscess of the brain from bronchiectasis or other pulmonary disease has long been recognized. Saelhof reports a case in which multiple bilateral brain abscesses were secondary to bronchiectasis caused by the wedging of the lower lobe of the right lung into a pocket formed by kyphoscoliosis. The causative agents isolated and cultivated from both the abscesses and the suppurating lung were *B. fusiformis* and anaërobic streptococci. The most probable route by which the infection travelled from its primary focus was the blood stream.

Inability to Recognize One's Own Blindness. It seems strange that a person may become blind and be entirely ignorant of this fact, and yet be entirely rational. Cases of this type have been observed in which the blindness came on gradually, but Bychowski²⁷ had the opportunity during the war to observe 2 cases in which the blindness came suddenly after an injury of the brain. One case is reported in detail. The man seemed to have been shot through both occipital lobes. The light reaction and the eyegrounds were normal, but the man was completely blind, and could not recognize an electric light. He asserted that he had no cause to complain of his eyes, as he could see everything, and yet if he were asked how many fingers were held before him he answered promptly but always incorrectly. Other tests similar to this yielded always incorrect answers. When given a book he explained his

²⁶ *Journal of Nervous and Mental Disease*, April, 1920, p. 330.

²⁷ *Neurologisches Centralblatt*, June 1, 1920, p. 354.

inability to read it by saying he had a headache, or it was too dark in the room, or he needed glasses, but always denied that he was blind.

The occipital lobes probably were separated by the injury from the rest of the brain. Bychowski compares the condition with that following amputation, when the person in whom a limb has been amputated still has sensation in the limb. Such a person corrects the illusion through touch and sight. If he were blind and unable to move his remaining limbs and were not aware of the amputation, probably he would deny that he had lost a limb if he were asked. A similar condition might result in one who had suddenly had his occipital lobes separated from the rest of the brain. The old optical impressions would remain in the visual cortex and as this cortex would be removed from all control by other parts of the brain the man would become mind blind to his own blindness. Usually in these cases there is much euphoria.

Intermittent Blindness. Attacks of blindness lasting a few hours are fortunately uncommon. Kurt Mendel²⁸ reported in 1916 an interesting case of this character. A man who had had an injury of the occipital region, only after moderate exertion or great excitement would be liable to have headache and general weakness and then objects would become indistinct. After fifteen or twenty minutes complete bilateral blindness would develop. If he laid down, the blindness would disappear after one to four hours. If he did not close his eyes the blindness lasted much longer, even a whole day. When he observed, by the beginning dimness of vision, that his attack was coming on, he sought his home during the fifteen to twenty minutes before he lost his sight completely. The attacks ended quite suddenly and were not accompanied by unconsciousness.

He now reports a similar case in a boy, aged thirteen years, in whose family there was no migraine. The attack began with pain in the eyes and dimness of vision passing in five minutes into complete blindness, which lasted fifteen to thirty minutes. The return of vision was sudden, and after sight began it was fully restored within one minute. No cause could be found for the attacks and they came suddenly.

Mendel explains these attacks of intermittent blindness as a result of exhaustion of the visual cortex; as an intermittent lameness of this area depending on vasomotor disturbance. He refers to no similar observations in the literature, but asserts that these attacks can have no relation with hysterical amaurosis.

Decerebrate Rigidity in Man. S. A. K. Wilson²⁹ has given us the results of careful and important observations in man on a condition analogous to that produced by experimental mesencephalic transection in apes and other mammals and known as decerebrate rigidity. Such cases in man are not very frequent. The type of case is one in which there is evidence of withdrawal of cortical control in the form of unconsciousness or semi-consciousness, the result commonly of cerebral hemorrhage, submeningeal or intraventricular, or both, or of meningeal inflammation, or from the effect of certain intracranial tumors, or even of hysteria.

²⁸ *Neurologisches Centralblatt*, 1920, No. 15, p. 503.

²⁹ *Brain*, 1920, xliii, part 3, 220.

Coupled with this impairment of consciousness is the appearance of tonic rigidity of trunk and limbs with exacerbations in the form of tonic fits.

In certain types of organic and functional nervous disease these postural attitudes may be adopted involuntarily with full consciousness, and partial or fragmentary types also occur. The transient positions assumed in involuntary movements, such as chorea or athetosis, may be simply parts of the complete decerebrate attitude. The description Wilson gives of a case is as follows: The upper limbs are rigid, adducted at the shoulder and strongly extended at the elbow, with pronounced internal rotation and hyperpronation; the wrists are flexed so that the palms of the hands are turned up and out. The lower limbs are rigid, adducted, extended, the feet are inverted and the great toes strongly dorsiflexed. In abortive cases where the condition is confined to a segment of a limb, the most important feature may be pronation and flexion at the wrist, and this is seen especially in cases of chorea or athetosis.

Congenital Word Blindness. The article by Wallin³⁰ on this subject has the importance of coming from the Director of the St. Louis Psycho-Educational Clinic and Special Schools. While this condition is recognized, the concept, as he says, has remained scarcely more than an abstraction, interesting as a theory but of little practical moment, to those who have studied pedagogically retarded children by measurement of intelligence by the Binet-Simon scale or group intelligence tests. Yet analysis of individual cases shows conclusively that some children fail to advance in school, chiefly because, owing to some degree of word-blindness, they are partially or totally unable to learn to read. Many word-blind children, normal or merely backward in intelligence, have been diagnosed as feeble-minded and assigned to special classes for mental defectives. Wallin has made an analysis of some of the data gathered in 95 consecutive cases from St. Louis examinees whose reading disability has been attributed to some form of word-blindness. The average chronological age of the group of word-blind children was 11.07, the average intelligence age 8.85. It is remarkable that word-blindness was about four times as prevalent among the boys as among the girls. This collection of word-blind cases is believed by the author to be the largest ever presented in the literature. Hinshelwood described a dozen cases in his treatise. He had observed 31 congenital and acquired cases in fifteen years. It is important to remember that many children with word-blindness have been normal in intelligence or even precocious.

Wallin states in a footnote that he believes auditory aphasia to be exceedingly rare. This opinion probably must be attributed to his material, certainly it is not exceedingly rare in brain disease, especially in tumor. It doubtless is rare in children. The recognition of word-blindness when it exists in children is of vast importance in the education of these children.

Global Aphasia and Bilateral Apraxia from Supramarginal Gyrus Lesions. Usually a tumor is hardly trustworthy for localization as it produces

³⁰ The Lancet, April 23, 1921, p. 890.

many symptoms by pressure, but the one removed by Cushing from the supramarginal gyrus and reported by Bremer³¹ has value. It measured 4 by 3.5 cm. and was an endothelioma, therefore not an infiltrating growth. The patient, a man, was entirely unable to understand speech although he occasionally recognized a word. He could write nothing except his name correctly. He also had bilateral ideomotor apraxia. When offered a familiar object such as a matchbox he would hide it in his bed, take it out and regard it with perplexity, put it on his head, or execute most absurd movements with it; for example, quick alternative flexion and extension of the elbow. When offered a cigarette and a box of matches together, he put the cigarette in his mouth but executed with the matchbox the same absurd movements. Marie and Foix have attributed this apraxia with global aphasia to a lesion of the left supramarginal gyrus, and associated with those symptoms are slight paresis of the right upper limb with marked sensory disturbances.

Syphilis of the Nervous System. Pette,³² using the material from Nonne's large service of syphilitic patients, has attempted to answer some of the important questions regarding syphilis of the nervous system. The questions for which he has sought answers are: (1) Can intensive treatment in the primary or secondary stage prevent the development of tabes and paresis? and (2) Does the length of the incubation period have any relation to the intensity of treatment? In the past ten years there have been 868 cases of tabes and 595 of paresis in Nonne's service, of this number 484 of tabes and 280 of paresis were suitable for study. Of these tabes cases, 315 had not been treated, 164 of the remaining had been treated with mercury, 5 had received both salvarsan and mercury. Pette concludes that vigorous treatment of syphilis in the primary or secondary stage is not always able to prevent the development of tabes or paresis. He finds that:

The great majority of tabes and paresis patients are in the syphilitic who have not been treated for this disease, the tabes patients without treatment amounted to 65.2 per cent, the paresis to 68.2 per cent, whereas the sufficiently treated amounted to 4.1 per cent and 1.1 per cent.

The earlier in life syphilis was acquired the longer was the incubation, and it diminished with increasing age.

The treatment with mercury could not be regarded as a cause for the development of tabes or paresis. He was not able to determine the degree to which salvarsan prevented the development of the diseases in question

Moore,³³ from his studies of cases in the syphilis department of the Johns Hopkins Hospital, in writing on syphilis, says it is undoubtedly true that a few patients in whom early invasion did not take place later fall victims to neurosyphilis, thus rendering necessary the assumption of nervous invasion at a second or later period of generalization of the disease. He takes, therefore, a little different view from that expressed by Fordyce, although he also believes that in most of those who later

³¹ Archives of Neurology and Psychiatry, June, 1921, v, No. 6, 663.

³² Deutsche Zeitschrift für Nervenheilkunde, Nos. 3 and 4, vol. lxvii, p. 151.

³³ Journal of the American Medical Association, March 19, 1921, p. 769.

develop neurosyphilis, invasion of the nervous tissue takes place early in the course of the disease, at the time of the first period of generalization. Examination of the spinal fluid in early untreated primary and secondary syphilis has shown from 30 to 50 per cent of abnormalities, consisting in general of pleocytosis and increased protein content, more rarely a positive Wassermann reaction and abnormal colloidal tests.

Previous to the introduction of the arsphenamin, the statistics of various observers indicated that only about 5 per cent of well treated patients, as compared with 25 per cent of untreated or badly treated patients, developed paresis, tabes or cerebrospinal syphilis. In the Johns Hopkins Clinic under the present intensive treatment the impression prevails that less than 1 per cent of well treated patients develop neurosyphilis.

Moore, from a study of 642 cases, concludes that if primary syphilis can be well treated before the appearance of secondary manifestations, only a very small proportion, 2.9 per cent of cases will show any abnormalities in the spinal fluid after treatment. He believes the value of intensive routine treatment as a prophylaxis against neurosyphilis is fully illustrated. He has found that asymptomatic neurosyphilis is approximately twice as frequent in white as in colored patients.

Involvement of the Nervous System During the Primary Stage of Syphilis. The period at which disturbance of the spinal fluid is present in syphilis is of much importance. Wile and Hasley³⁴ report their results in the study of 221 cases of syphilis in which only the primary sore was present. The early period at which these cases were studied is indicated by the fact that of this number, 106 gave negative findings in the blood.

Of the total number of cases studied (221), a deviation from arbitrary normal criteria (eight cells, negative Wassermann test, etc.) was found in 60. Of this number, 11 cases showed merely an increase of one or two cells above the arbitrary normal of eight, and it may be justly contended that on such basis involvement cannot be said to be definite. In the remaining 49 cases, definite involvement of the nervous system could be properly assumed on pleocytosis, increased solids, and positive Wassermann test, although not all of these findings were present in each case. Increased albumin and globulin, virtually parallel, were found in 25 cases, pleocytosis in 12, and positive Wassermann test in 8 cases. Of the entire number of cases examined, symptoms indicating central nervous involvement were present in only a single case, in which continuous headache, extending over a week's time, was found in association with positive findings throughout in the spinal fluid.

These investigators conclude that within certain limitations any single one of the above-mentioned deviations from the normal occurring alone must be regarded as evidence of early central nervous system involvement.

Treatment of Neurosyphilis. The views of Fordyce³⁵ as to the importance of preventing the development of syphilis of the nervous system by the early treatment of a syphilitic infection are emphatic, quite different

³⁴ Journal of the American Medical Association, January 1, 1921, p. 8.

³⁵ American Journal of the Medical Sciences, March, 1921, p. 313.

from those held by some other observers as regards the preventive efficacy. He says that the fate of a syphilitic individual as regards his future immunity to neurosyphilis rests largely on the result of a spinal fluid examination, either during his treatment or before his final discharge, and, if infection is present, on its complete clinical and serologic cure. Both the patient and physician are too often satisfied with a symptomatic cure and a disappearance of the obtrusive signs. He believes there are superficial types of neurosyphilis which are readily curable in the early stages as shown by the condition of the spinal fluid; and other deeper types which yield only to prolonged treatment. The latter in their therapeutic response and fluid formula are probably of the preparetic type which without treatment would eventually result in degenerative encephalitis. He believes that practically all types of neurosyphilis originate within the first year of the infection, and are then amenable to properly applied therapeutics.

He also believes in a strain of the treponema with neurotrophic affinities, and because of its greater invasive power or its attraction to nerve tissues it implicates these structures early in the infection in about 25 per cent of all cases of syphilis. He insists on spinal fluid examination before he is willing to pronounce a cure. If the spinal fluid is negative in all its phases after the other criteria of cure are complied with, he feels he can assure his patient, with a considerable degree of confidence, that he need have no fear of late neurosyphilis. It is strongly probable, he believes, that the treponema invades the nervous system during the period of general dissemination or not at all. He acknowledges, however, we have not yet sufficient data to deny absolutely the possibility of infection of the nervous system later than the early florid stage, but he thinks such infection extremely improbable. Properly employed therapeutic procedures controlled by examinations of the spinal fluid, he asserts, cure practically all cases of early neurosyphilis. In none of the cases cured serologically and clinically has he seen later active recurrences. He goes so far as to express the belief that it is possible to eradicate absolutely the most feared of all the results of the disease.

Fordyce has examined and treated a number of cases in which previously spinal drainage combined with intravenous treatment had been employed. In the majority, aside from minor changes in the cytology of the fluid, no improvement was observed. He contends that after failure by the intravenous route we have a valuable procedure in the intraspinal method when used with the proper technic and where indications are present for it. The intraspinal treatment is contraindicated where there is clinical and serologic response to the intravenous mode of administration and in all cases with negative findings in the fluid even though clinical signs may be present.

He says no serologic evidence as yet exists showing normal spinal fluid in the early stage and infection of this fluid at a later period. He is convinced by an experience of seven years in the use of intraspinal therapy that practically all cases of early neurosyphilis can be cured more rapidly, and the majority of cases cured, only by the combined intravenous and intraspinal method.

Extradural Spinal Injections for Syphilis. Fifteen cases have been treated by Farnell³⁶ within a year by injections outside the dural sac. These were early cases of tabes where the response to intravenous injections was poor, special cases of early syphilis of the cord, fairly advanced cases of combined sclerosis from syphilis, early cases of multiple sclerosis, and cases of the exudative form of meningo-encephalitis.

The treatment is supposed to avoid the puncture headache and to make remaining in bed after the injection unnecessary. It occurred to Farnell that it might be possible to utilize the large extradural space which contains great amounts of areolar tissue well vascularized and containing many lymphatics. He injected salvarsanized serum into this space without removal of spinal fluid.

All his patients received a lumbar puncture in order to diagnosticate their condition clearly. By the extradural treatment approximately 70 per cent improved rapidly, so that after ten to fifteen injections they were considered not only free from the symptoms of which they primarily complained but also showed a change in their neurophysical complex. Three patients who were considered well enough to cease treatment showed a negative blood and spinal fluid for the Wassermann reaction.

Spinal Drainage in Treatment of Syphilis. This method has received some adverse criticism presented in an article by Stokes and Osborne.³⁷ They also have made investigations concerning it by placing 50 patients with neurosyphilis on spinal drainage. Their method consisted of weekly withdrawal of from 30 to 70 cc of spinal fluid from fifteen minutes to one hour following an intravenous injection of arsphenamin. Mercury, in the form of inunctions or the intramuscular injection of a soluble salt, was also employed in every case. Only 25 of the 50 patients received sufficient treatment to be included in their statistics. The average number of spinal drainage in each case was five, the highest number being nine and the lowest three. On the completion of drainage the patients were placed on interim inunction treatment and reexamined after intervals of from two to nine months. The somewhat disappointing results led to their being placed on Swift-Ellis-Ogilvie intraspinal treatment. These writers state they have ceased to place any great reliance on spinal drainage.

They found that a transient but marked rise followed by a fall toward normal limits occurred in patients receiving spinal drainage, and they believe that a similar Herxheimer-like curve of pleocytosis accompanied by transient exacerbation of symptoms occurs in many patients under treatment for neurosyphilis by routine methods. Temporary rise in the cell count early in the course of treatment should not, therefore, necessarily be regarded as of unfavorable prognostic significance.

Juvenile Tabes. The report of Parker³⁸ on juvenile tabes is chiefly remarkable in the comparatively large number of cases of this form of tabes from one clinic collected within three or four years. He reports

³⁶ *Journal of Nervous and Mental Disease*, May, 1920, p. 420.

³⁷ *Journal of the American Medical Association*, March 12, 1921, p. 708.

³⁸ *Archives of Neurology and Psychiatry*, No. 2, vol. v, p. 121.

10 cases studied in the Mayo Clinics, the first was seen in 1916, but he gives condensed notes of only 7. Early tabes is usually considered more uncommon than this number would imply. He mentions as characteristic of the early form: The insidious onset, the lengthy and even latent course of the disease, when no subjective disorder may be noticed, although optic atrophy and even total blindness may occur. Also characteristic are the frequency of incontinence of urine, the relative rarity of such striking phenomena as ataxia, girdle sensations and lightning pain, and finally the frequent paretic termination.

Familial Tabes Dorsalis. One may be pardoned for entertaining some skepticism as to the occurrence of tabes dorsalis as a family disease, and therefore Burrow's³⁹ paper will be viewed with some caution. He describes a family in which of 6 surviving members from 8 children, born of parents supposed to be healthy, 4 had acquired undoubted syphilis from different sources, with resulting tabes dorsalis in all. A fifth member of the family acquired gonorrhea but syphilitic infection was regarded as doubtful, and yet he was thought to have early tabes. A sixth escaped venereal infection and remained healthy.

It is suggested by Burrow, on the strength of these facts, that tabes cannot be attributed to a special strain of spirochete introduced at the initial infection, but is much more likely to be caused by the spirochete acting upon tissues specially sensitized, either by natural family peculiarity or by certain methods of treatment.

The discovery of the spirochete in the tissues (brain and cord) of general paralytics and tabetics he thinks should stimulate further research into the other, still unknown, factors which are concerned in the production of these diseases.

There seems to have been no examination of the father of this family, and he was dead at the time the children were examined. The mother showed no physical sign of disease and was ninety-two years old, but evidently no laboratory tests were made in regard to her. Four of the members of this family had tabes in an advanced form and the diagnosis of this disease seems unassailable, the fifth member had less pronounced symptoms and the diagnosis of tabes might be questioned. There seems to be no reason why syphilis should be considered improbable in this case. No laboratory tests were made and the man had had three attacks of gonorrhea. Many a syphilitic patient has no knowledge of his infection.

The occurrence of 4 cases of advanced tabes in one family, even though syphilis was believed to have been contracted by each of these four members, is a very extraordinary finding.

Pseudo-tabes Spondylosique. Rigidity of the spinal column with ankylosis of the joints in the proximal parts of the limbs is not usually difficult to diagnose, but in the early stage before these signs appear the symptoms may suggest tabes, and Babinski has employed the name mentioned above. Ganter⁴⁰ describes a case of this kind in which the patellar and Achilles reflexes were lost, and pain and atrophy were

³⁹ Journal of Neurology and Psychopathology, No. 3, vol. i, p. 246.

⁴⁰ Deutsche Zeitschrift für Nervenheilkunde, Nos. 1 and 2, vol. lxxvi, p. 16.

present in the lower limbs, before symptoms of involvement of the spinal column appeared. The loss of reflexes and the pain were attributed to the implication of the roots in the intervertebral foramina and the atrophy to inactivity. The absence of ocular and other symptoms of tabes should make one cautious in the diagnosis of such a case.

Pseudo-tabes following Head Injury. Some types of nervous disease resembling in a few symptoms tabes have been reported, but usually careful study has made it possible to distinguish between these and true tabes. The peripheral pseudotabes is the best known. Oppenheim has described a form of pituitary disease giving symptoms resembling those of tabes. Roemheld⁴¹ now describes what might be called a near-tabes following head injury. Syphilis seemed to be excluded, and the laboratory findings were negative. The pressure of the cerebrospinal fluid was considerably increased and suggested a serous meningitis, possibly associated with multiple areas of small hemorrhages and softening in the brain, caused by the trauma.

A patient Roemheld describes had the subjective and objective symptoms of a severe cerebral commotion, and tabetic symptoms, as prompt pupillary reaction in the right eye but incomplete rigidity of the pupil in the left eye, the left pupil scarcely contracted at all to light and was very sluggish in convergence and accommodation reaction. There was labyrinth disturbance greater on the left side. The left patellar reflex and both Achilles reflexes were absent, and the right patellar reflex was very weak. Pain sensation was lessened. Four years later the right pupil was found to be rigid, and a myotonic character of this pupil was observed. Twelve seconds were necessary for the maximal contraction in convergence and sixty seconds for the following dilatation after convergence had ceased. Accommodation tonia was annoying, eight to ten seconds were necessary after the man had looked into space before he could read fine print.

The symptoms of this pseudotabes consisted of rigid pupils and loss of tendon reflexes, but there was the history of head injury and headache, vertigo and what Roemheld calls "intolerance" of the brain. Saenger, in discussing this report, remarked that ophthalmoplegia interna is usually a late sign of syphilis and seldom the result of direct injury of the eyes. Even though the laboratory findings were negative, he recommended antisyphilitic treatment. Otto Maas shared this opinion, and asserted that negative findings do not exclude syphilis. This view can be readily accepted.

Family Spastic Paralysis of Syphilitic Origin. Family spastic paralysis from any cause is rare but the possibility of heredosyphilis in some of the cases of this disease has been recognized. Mingazzini⁴² has published an interesting paper on this subject. He has found that clinical histories of cases of this type have been published only recently. Nonne has collected about 10 cases in his book. Mingazzini now gives the clinical histories of 3 such cases occurring in two brothers and a sister, the offspring of a syphilitic father, who had tabes. With the exception

⁴¹ Transactions of the Society of German Neurologists, 1920.

⁴² Archives of Neurology and Psychiatry, June, 1921, No. 6, v, 637.

of the first-born, all of his children were more or less deficient; all three, at about puberty, began to show progressive motor disturbances of the lower limbs terminating in the syndrome of family spastic paralysis. One of the brothers also had optic atrophy, choroiditis and double cataract. Mingazzini gives references to a fair number of similar cases, and from all of these he makes a clinical grouping.

The first signs of the spastic spinal syndrome caused by heredosyphilis may manifest themselves just as the child begins to walk; locomotion may begin normally or be retarded; in other cases the first signs appear after the child has learned to walk properly. In Nonne's first case the onset was at the age of four, in Mendel's at five, in Dejerine's at eight, in Hoffmann's at twelve, and in Mingazzini's at puberty.

The motor paralysis may be limited to the lower extremities, or it may extend to the upper extremities. The paresis and spasms were sometimes uniform, rarely severe enough to prevent the patient from standing up. The spasms have a gradual onset and sometimes attain a severe degree of rigidity; sometimes even extension contractures of the thighs and legs and plantar flexion of the feet have been present. In 1 case spasm of the muscles of the neck was found. The reflexes of the lower extremities usually are exaggerated and ankle clonus may be present. In many patients the pupils did not react to light. General sensibility is usually well preserved.

Psychic disturbances were common but none seemed to attain a severe degree, but in some cases varying degrees of imbecility were present. The Wassermann reaction has been positive in some cases and negative in others. Mingazzini thinks an important factor in the production of the disorder is the lack of antisiphilitic treatment in the parents. It is not unreasonable to suppose that many of the cases of family spastic paralysis, described at a period when syphilis was not carefully considered, are really caused by heredosyphilis. It is hard to say under what conditions heredosyphilis will produce spinal spastic paralysis rather than some other type of cerebral or spinal disturbance.

The Treatment of Spastic Gait by Permanent Flexion of the Toes. As spasticity of the lower limbs can be overcome temporarily by bending the big toe downward, as first shown by Sinkler, it occurred to me that by keeping the toes partially flexed, as by a bandage or properly adjusted shoes, it might be possible to make a person with a spastic gait walk in a more normal manner, and I⁴³ demonstrated a case of this kind before the Philadelphia Neurological Society recently. The boy dragged his toes in his very spastic gait. This was demonstrated. The feet were then bound with adhesive plaster with a small roller bandage under the toes, so as to keep the toes partially flexed. The result was striking. The boy immediately raised his knees abnormally high. By properly adjusting the degree of flexion of the toes, it was possible to make the gait more nearly normal.

When the reflex of defense exists, it can be produced voluntarily by flexing the big toe. This movement causes a contraction of the flexor

⁴³ Archives of Neurology and Psychiatry, June, 1921, No. 6, v, 771.

muscles of the lower limbs. It is a well known law, emphasized especially by Sherrington, that contraction of one group of muscles produces relaxation of the opposing group. By producing a persistent slight contraction of the flexor muscles by keeping the toes properly flexed, it appeared that the extreme spasticity of the lower limbs in extension could be overcome. This method of treatment needs further study, and it is a question whether the reflex produced in this manner would become exhausted.

External Spinal Pachymeningitis. An unusual pathological finding, and one which would be very difficult or impossible to diagnose from the clinical manifestations, is reported by Fuchs.⁴⁴ Granuloma tissue on the outside of the dura extended from the sixth to the ninth thoracic vertebra, and was very vascular and did not invade the interior of the dura. A similar condition was found in the pleura and peritoneum, but only the lesions of the dura produced symptoms and these were very diffuse. The diagnosis was made of polyserositis chronica fibrosa or hyperplastica with metastasis to the outer surface of the dura, where the lesions evidently were of more recent date, and caused symptoms of pressure upon the cord. Nothing specific could be found in these lesions. Extradural spinal tumors and inflammations are not as frequent as intradural, and their symptomatology is not so well understood. Some of these offer better surgical opportunities than do the intradural lesions.

Multiple Sclerosis. The experiments of Kuhn and Steiner have been repeated by Rothfeld, Freund and Hornowski⁴⁵ in the attempt to demonstrate a spirochete as the cause of multiple sclerosis. They had examined preparations sent by Steiner and were able to see the spirochetes in great numbers in the liver and vessels of rabbits in these preparations. They made very careful study of their own work and yet were not able to find spirochetes in their experimental animals in the nervous system, viscera or vessels, although they employed different methods and examined the blood of the animals almost daily. Their negative results led them to conclude that the spirochetes observed by Kuhn and Steiner were not specific for multiple sclerosis and were contaminations transmitted from animal to animal. Kuhn and Steiner had considered this possibility but had dismissed it.

Cerebrospinal Fluid in Multiple Sclerosis. In a study of the spinal fluid in multiple sclerosis, D. K. Adams⁴⁶ has obtained some interesting results. He has regarded as suitable for investigation:

1. Cases showing spastic paraplegia, absent abdominal reflexes, and one or more of the other classical signs of multiple sclerosis.

2. The primary lateral sclerosis or spastic paraplegia group with a negative Wassermann reaction, a positive colloidal-gold reaction, absent abdominal reflexes, and the absence of any sign of other organic disease.

3. Cases of spastic monoplegia giving a luetic curve to colloidal-gold in the cerebrospinal fluid, with a negative Wassermann reaction and no signs of other organic disease.

⁴⁴ Deutsche Zeitschrift für Nervenheilkunde, Nos. 5 and 6, vol. lxvi, p. 231.

⁴⁵ Ibid., vol. lxvii, p. 257.

⁴⁶ The Lancet, February 26, 1921, p. 420.

4. Cases of primary optic atrophy with a negative Wassermann reaction in blood and cerebrospinal fluid.

Adams concludes:

1. The cerebrospinal fluid picture in multiple sclerosis is as follows: a normal cell count, a negative Wassermann reaction, a luetic or parietic reaction to colloidal gold, and in most cases (83 per cent) a normal protein content.

2. The absence of a positive Wassermann reaction in the great majority of cases and the absence of pleocytosis are in accordance with the view that this disease is not of syphilitic origin.

3. On the supposition that the origin might be spirochetal treatment was carried out by spirocheticidal drugs. In practically every case under treatment, modifications toward a negative result of the colloidal-gold reaction were noted.

4. As regards clinical effects of such treatment, no improvement resulted in advanced cases of the disease, but prolonged treatment produced amelioration of early cases, and in one or two instances the results were marked.

5. With reference to early diagnosis, emphasis is laid on the evidence of the cerebrospinal fluid picture and the absence of the abdominal reflex.

Central Pain of Spinal Origin. In my digest of last year I called attention to Holmes' important paper on this subject in the volumes dedicated to Sir William Osler. The paper evidently has escaped the eye of Lhermitte⁴⁷ who writes on the same subject. He divides the cases into three groups: (1) The radicular type, (2) the hyperalgesic type, and (3) the causalgic type. Babinski and Dubois have spoken of the severe pains occurring in what the French have called "commotion" of the spinal cord under the designation of pain of the type of electric discharges.

The radicular type is usually observed in commotion of the cervical cord causing grave symptoms, as in monoplegia or diplegia. Those having brachial diplegia from a wound of the cervical cord may have paroxysms of intense pains by day and night which are described as burning, as resulting from twisting of the arms, etc., and morphia may be needed to quiet them. The pains may not be confined to any anatomical distribution but often they follow the cervical roots, especially along the posterior surface of the arm and the external border of the forearm. Movement of the paralyzed upper limbs, rubbing the skin, or even light touch may arouse these paroxysms of pain.

Such pains as these are less frequent in commotion of the thoracic region, and, when present, have a girdle form as in tabes, and may be increased by sneezing. Usually these radicular pains are associated with very slight objective disturbance of sensation, and though the pains often persist a long time they disappear gradually in the course of months.

In the hyperalgesic type, spontaneous pains are slight or even absent, but the skin of the paralyzed limbs as of the upper limbs and even of

⁴⁷ *Revue Neurologique*, 1920, No. 3, p. 257.

the lower limbs and trunk, is extremely sensitive to rubbing or pinching in the cervical commotion. The cutaneous hyperalgesia may make it difficult for the patient to endure the pressure of the chair in sitting. It has been observed also in commotion of the thoracic or lumbar region. The hyperalgesia may be present in the urethra, making catheterization difficult.

The causalgic form fortunately is rare; and only one case has been observed by Lhermitte. The pain is that of intense burning. Involuntary jerking of the paralyzed limbs may increase or start the pain anew, or even rubbing or pinching the limbs may have the same effect.

The pains of the type of electric discharges develop late and are like the sudden onset of a current of electricity. They are very often in the lower limbs, or may be in the hemiparetic side of the body, and are always provoked by flexion of the head or trunk, which fact is recognized by the patient and this movement is avoided. The prognosis of this form of pain is good, as recovery is likely to occur.

These various forms of pain cannot be attributed to the same cause. The root pains must be caused by root irritation, but the hyperalgesia or spontaneous pains affecting all the body below the level of the lesion, if caused by root involvement, would imply that all the roots from the cervical to the lower sacral region were involved, which is not probable and such a theory may be rejected. These pains must be from the lesion of the spinal cord, and occur also in affections of the cord like myelitis, intramedullary tumor and syringomyelia. The sensations of electric discharge must have a similar origin, and just as percussion or stretching of a peripheral nerve undergoing regeneration causes a sensation which the wounded compare to an electric shock, so the spinal cord undergoing regeneration, stretched by the flexion of the trunk or of the head, may give rise to similar sensations. The fact also that these pains, unlike those of the other types, develop late is believed by Lhermitte to support him in his interpretation.

Cerebrospinal Fluid in Compression of the Spinal Cord. Raven has studied the syndrome described by Nonne and Froin from the cases in Nonne's clinic and from those reported in the literature. Nonne found in 1908 that a considerable increase of albumin of the spinal fluid without increase in the cells was characteristic of compression of the cord. Froin in 1903 had determined a similar condition consisting of rapid coagulation of the fluid rich in albumin and with xanthochromia. Raven¹⁸ concludes:

That isolated phase 1 of the Nonne reaction occurs very seldom with intramedullary tumors and somewhat more frequently with extradural than with intradural tumors.

Xanthochromia is not characteristic of compression of the lower portion of the cord, its frequency increases in compression from upper toward lower levels, whereas isolated phase 1 diminishes from upper toward lower levels.

Xanthochromia does not indicate whether a tumor is intramedullary or extramedullary.

¹⁸ Deutsche Zeitschrift für Nervenheilkunde, Nos. 1 and 2, vol. lxxvii, p. 55.

Rapidly increasing severe compression seems more likely to cause xanthochromia than slowly increasing pressure.

Spontaneous coagulation is observed chiefly with extramedullary intradural tumor.

The level of compression is unimportant for the intensity of the changes in the fluid.

The character of the compressing tumor is without influence on the development of the different changes in the spinal fluid.

Remission in Spinal Cord Tumor. An extraordinary case of partial recovery in a case of tumor of the spinal cord is reported by Jumentié.⁴⁹ Improvement in symptoms with tumor of this character is not common, and it is extraordinary that the period of improvement could be so long as in Jumentié's case. No explanation is offered.

A woman was admitted to the hospital in 1905, with paralysis of the lower limbs and weakness of the upper. She was very anemic. The paralysis had commenced in one lower limb, and violent pains were felt in the lower limbs, and these limbs became almost completely paralyzed. The upper limbs showed atrophy and reaction of degeneration. The tendon reflexes of the upper limbs were abolished while those of the lower were much exaggerated. The symptoms were those of tumor of the cervical region of the cord. Improvement then began, progressed very slowly, and the woman left the hospital in 1908. She was able to walk with crutches and had recovered full power in her upper limbs and control of the sphincters. She was able to resume her occupation of baking. In 1911, the symptoms returned and she became confined to bed, her condition became the same as at her previous admission to the hospital, and death ensued.

An intradural tumor was found on the cord in the cervical region, and it had caused much atrophy of the left half of the cord near the tumor. It was diagnosed as fibromyxosarcoma. The lesion had been supposed to be tuberculous pachymeningitis, and this diagnosis had been strengthened by the long period of recovery. Operation evidently was not performed. Such a case as this must put us on our guard in diagnosis, for operation is demanded and is likely to be omitted.

Amyotonia Congenita. The distinctions between this form of disease and the Werdnig-Hoffmann type of atrophy have been indefinite. Krabbe⁵⁰ makes the following comparisons:

1. Amyotonia congenita, according to the original descriptions, seems to be rather benign and not a hereditary disease, and does not seem to leave any defect in adults.
2. In 8 of the 11 cases which have come to autopsy, there have been severe atrophies of the anterior horn cells and muscles.
3. In 2 of Krabbe's cases of hereditary congenital muscular atrophy, corresponding changes were seen.
4. These changes resemble, on the whole, the changes in the Werdnig-Hoffmann progressive muscular atrophy.
5. In his 6 cases the disease clinically resembled closely amyotonia

⁴⁹ *Revue Neurologique*, 1921, No. 3, p. 285.

⁵⁰ *Brain*, vol. xliii, Part II, p. 166.

congenita, and only later information showed that it was a familial disease.

He believes the cases which have been described as amyotonia congenita represent two different diseases:

1. One of these, amyotonia congenita is a benign disease, which consists of a congenital hypotonia, hyperflexibility and weakness, but no atrophies. If the patient does not die from intercurrent disease, it may be assumed that he is cured. It is not familial and can possibly be considered as a retarded development of muscles.

2. From this true amyotonia congenita must be separated the condition described in a considerable number of the cases in literature, which must be considered as cases of congenital familial progressive spinal muscular atrophy, a type which is most related to Werdnig-Hoffmann's type, but is congenital. This disease has a certain clinical resemblance to amyotonia congenita, but differs from it in that the muscles show a marked atrophy, demonstrable by the x-rays, and in that it has a tendency to progression or at any rate not to improvement, and in that, for a certain number of cases, it can be shown that the disease is familial. This is a point of view I have held for some time, as the pathological findings in the 2 cases I studied from necropsy were totally different.

Hoffmann up to the time of his death had collected 11 cases of myotonia, of which 2 were with necropsy, and these are now reported by one of his pupils, Arthur Slauck.⁵¹ The latter states the disorder may be congenital or acquired very early in life and shows usually a tendency to increasing severity, although many observers speak of a favorable prognosis. The improvement, however, may be more apparent than real, as the child as it grows older learns better how to use its impaired muscular power. The numerous deaths from intercurrent disease is also evidence of the bad prognosis, as is also the lack of cases in adults who have outgrown the disease. A family type has not been generally recognized, but Slauck reports two families in which the disease occurred.

Hoffmann observed frequently fibrillary tremors of the tongue. In 4 of the cases contractures were observed. In the two necropsies the findings were primary degeneration of the cells of the hypoglossus nucleus and of the anterior horn cells in the cord, with changes in the anterior roots. These are the findings of progressive spinal muscular atrophy. Slauck believes different affections have been described under the name of myotonia. He does not report recovery in any of his cases, and he does not make a sharp differentiation between myotonia and the Werdnig-Hoffmann atrophy.

Section of the Antero-lateral Columns of the Spinal Cord for the Relief of Pain. Frazier⁵² has performed this operation for the relief of pain in the lower part of the body in 6 cases.

CASE I was one in which an inoperable sarcoma of the spine was found at the level of the second and third lumbar vertebrae. Suffering was intense and uncontrolled by morphine. Chordotomy was employed with section of both antero-lateral columns at the level of the first

⁵¹ Deutsche Zeitschrift für Nervenheilkunde, Nos. 1 and 2, vol. lxvii, p. 1.

⁵² Archives of Neurology and Psychiatry, 1920, No. 2, iv, 137.

lumbar segment. This resulted in total loss of thermal and pain sensations. Resections of the affected posterior roots would have been possible in this case, and indeed this procedure has been followed by Frazier in other cases, but he prefers the section of the antero-lateral columns. Rhizotomy, as he emphasizes, may permit the return of pain in cases of inoperable tumors by the invasion by the growing tumor of the roots above or below those divided at the operation. Chordotomy also is easier of execution than rhizotomy. No matter what the lesion is or where it is located, the operation implies the exposure of but one spinal segment, and the operator may select the segment at which the cord section is to be made. Frazier has chosen the sixth thoracic segment as being in a region of the vertebral column at the apex of its normal convexity and where it is readily accessible. •

CASE II was one of gunshot wound of the spine with intense pain in the left lower extremity. Four grains of morphine a day were given with only partial relief. Unilateral chordotomy was performed and resulted in complete cessation of pain. There had been no recurrence at the last observation twelve months later. The immediate withdrawal of the morphine after the operation from a patient addicted to large doses, was a striking and assuring demonstration of freedom from pain. The patient gained in weight, he was soon able to go about in a wheel chair, and he was transformed from a person in abject misery to a reasonably cheerful man, despite his other disabilities.

CASE III was one of carcinoma of the rectum, with pain in the rectum, buttocks and thighs. Bilateral chordotomy caused complete loss of thermal and pain sensations on one side. Radium therapy was employed for the carcinoma. Four years later the patient reported himself as free from discomfort. This case was remarkable in the extraordinary improvement after the use of radium. Four years after this treatment a previously bed-ridden patient was at work and had been able to ride a bicycle a great deal without discomfort.

CASE IV was one of inoperable sarcoma of the thigh with pelvic metastasis and insufferable pain in the gluteal region. Bilateral chordotomy gave relief from pain from the time of the operation until the patient's death several months later. The propriety of any operation where the expectation of life is brief might be questioned, but Frazier has no hesitancy under similar circumstances in recommending a chordotomy, especially as no risk is entailed and it assures the patient an extraordinary measure of relief from pain for the months that remain to him.

CASE V was one of gunshot wound of the spine with pain in both lower extremities. Chordotomy gave loss of pain and temperature sensations. The subsequent course was not known as the patient was a soldier and was lost to sight.

CASE VI was one of shell wound of the pelvis with injury of the sciatic nerve. Unilateral chordotomy gave great relief from pain for a considerable time, but later pain returned, probably because the operation was not sufficiently extensive. One must be cautious in performing this operation where paralysis of the lower limbs does not exist and he is likely to cut too little of the cord.

In the discussion of this paper, I⁵³ mentioned that the great danger in this operation is the involvement of the pyramidal tract, because, if cut, paralysis will result. It is not an operation which a surgeon should undertake unless he has had considerable experience in the surgery of the spinal cord, because it is an exceedingly delicate one. If the pyramidal tract were damaged slightly, permanent disability might not result, but it is not an agreeable thought that one has been the cause of producing paralysis in the lower limb of a man who had no paralysis, or only a little, before operation.

The fibers of pain and temperature probably are not in Gower's tract, but lie rather interiorly, and often the surgeon does not cut a sufficient number of these fibers to produce the loss of sensations of pain and temperature. I fail to see any reason, if the division in the cord is made in the thoracic region, why a surgeon should not cut nearly to the anterior horn, and even if he should cut a part of the anterior root at this level he probably would not do harm. The nerve cells in the thoracic region are not so numerous as in the cervical and lumbar regions, and the cutting of the anterior horn in the thoracic region, or even a part of the anterior root, probably would not produce permanent disability. One cannot cut an entire anterior root here by this operation, because the filaments of any one root of a thoracic segment extend over a considerable area of the spinal cord. At most, one can only cut a few of these filaments. The possibility of intramedullary hemorrhage must be considered.

Rupture of the Spinal Cord in Dystocia. The case reported by Kooy⁵⁴ is a remarkable example of this rare condition, and is spoken of by him as unique, as it deals with an almost total rupture of the spinal cord, while the child survived the trauma for nearly nine years. The rupture was at the level of the ninth and tenth thoracic segments. The child was born by version and extraction, the shoulders were delivered by the method of Müller. She had paraplegia, except for some flexion at the hip joints, she had also total or almost total loss of sensibility of the legs, incontinence of bladder and bowels, and decubitus in the sacral region. This case Kooy believes demonstrates the danger which is always inherent to strong traction during delivery, and the method of Müller, by which a deviation of the traction axis from the longitudinal axis of the child is brought about, may be considered especially dangerous.

When the spinal dura was cut the meninges were found fused with the cord at the level of the seventh thoracic vertebra, and surrounded the cord as a thick solid fibrous ring. Nearly the whole of the spinal cord had disappeared in the lesion and a transverse microscopical section showed fibrous tissue, with small isles of glia containing fibers and darkly stained cells. The ventral pyramidal tract was the only long tract left intact, and it was supposed that through this the flexion at both hips was possible.

Extradural Thoracic Abscess Secondary to a Boil of the Neck. It is important to recognize that a boil of the neck, if it penetrates deeply, may implicate the vertebral column. Pus may descend by gravity

⁵³ Archives of Neurology and Psychiatry, 1920, No. 5, iv, 575.

⁵⁴ Journal of Nervous and Mental Disease, July, 1920, p. 1.

until it reaches an obstruction and may give origin at this place to an abscess. As this secondary abscess may form some time after the boil of the neck has disappeared, the connection between the two may be overlooked. A case of this kind has been recorded by Wright and myself.⁵⁵ A man developed severe pains about the trunk and became completely paralyzed in the lower limbs for motion and sensation. As I had seen at least two other cases of this character and knew that a severe boil of the neck had occurred before any other disorder, I felt that an extradural abscess was pressing on the cord. This opinion was strengthened by the finding of the Nonne-Froin complex by lumbar puncture. The level of the lesion could be accurately determined and a puncture at this level revealed pus. Laminectomy then performed permitted the escape of a considerable amount of pus. Unfortunately, this operation did not arrest the course of the disease and the case terminated fatally.

Brain Complications in Measles. Fortunately, any involvement of the brain in measles is rare. Skoog⁵⁶ finds from a study of the literature that it is more frequent in children than adults and during the convalescence than during the febrile or exanthem stage. Most of the cases found in literature may be grouped under three or four headings. The meningitis group has a larger number than any other. Skoog reports 2 cases, one a cerebellar and the other a meningeal involvement.

The patient was a girl, aged four years. The mother noticed about the twelfth day of the measles and during convalescence that the child did not use her hands properly and was unsteady when playing with toys or performing any voluntary act. Walking was impaired and in a short time she could hardly get about. All deep reflexes were slightly increased, and the voluntary movements of the hands were so ataxic she could scarcely hold and drink a glass of water. All the movements were cerebellar in type. Seven weeks after the onset of these symptoms almost no trace of the clinical signs of involvement of the nervous system were present.

The second case also was in a girl, aged four years. She became entirely helpless and speechless, and recognized no one. There was present much motor unrest, with constant purposeless movements of hands and feet, but no true palsy. The case was regarded as one of meningitis associated with cerebritis, and it was considered reasonably certain that imbecility would always be present.

Chicken-pox and Herpes. In my digest of last year in *PROGRESSIVE MEDICINE*, I spoke of the possible relation between these two disorders. James Taylor⁵⁷ has written on this subject and returns to it in a recent paper. The evidence is accumulating. In his former paper he referred to several instances of chicken-pox occurring in the same house in which herpes had been present at, or about, the time at which chicken-pox occurred. In all the cases which had come under his observation or of which he had authentic first-hand information, herpes had occurred in

⁵⁵ Archives of Neurology and Psychiatry, January, 1921, No. 1, v, 107.

⁵⁶ Journal of the American Medical Association, June 19, 1920, p. 1697.

⁵⁷ British Medical Journal, September 18, 1920, p. 436.

an adult and had been followed by chicken-pox in younger persons, chiefly children. He has received some interesting communications which he publishes. This is hardly the place to give these letters in full but one may be quoted as an example. It was written by Dorward Brown, of Harrowgate. He says:

"A month ago I had a severe attack of shingles, radiating from the second, third, and fourth dorsal areas across the back and under the axilla to the sternum. A fortnight afterward my daughter, aged eleven, had a mild attack of chicken-pox. During my attack of shingles I also had some isolated vesicles scattered over various parts of my body. Following up this I found that a lady whom I was attending for shingles just before my own attack had been in contact with a family with chicken-pox. Lastly, I was consulted a few days ago by a patient from Bournemouth who has had an attack of herpes, and he informs me that his son and housekeeper followed him with chicken-pox."

Taylor thinks these instances furnish very strong evidence of the close connection between shingles and chicken-pox, and he supports Le Feuvre, who seems to have been the first to notice this connection, in his opinion that shingles should be recognized as an infectious disease, and one, under certain unknown conditions, likely to become a starting point for a chicken-pox epidemic.

Sympathetic Disturbance of the Upper Limbs from Midthoracic Lesions. The disturbance of sensory, motor and vasomotor function in the upper limbs from lesions of the middle or lower thoracic region has been called attention to by Barré and Schrapf.⁵⁸ They vary in different cases and in intensity, and may occur with mild or severe lesions of the cord. They may be so severe that the diagnosis of extension into the lower cervical region may be made, when in reality the part above the midthoracic region is intact. These symptoms do not appear to be very rare.

Barré and Schrapf believe, from their examination of the literature, that they are the first to describe this symptom-complex, although certain physiologists, especially Vulpian, have recognized its possible existence. Cases of soldiers wounded by a bullet or fragment of shell in the lower thoracic spine have been especially of value in illuminating the subject. As an example: a soldier was injured by a piece of shell passing through the spinal column at the eleventh thoracic vertebra, he complained of numbness on the inner part of each upper limb and the flexion of the fingers was feeble. The necropsy showed that the cord above the tenth thoracic segment was intact.

The symptoms are: paresthesia in the fingers of the ulnar side of the hand, usually of each hand, rarely pain, and more pronounced in the little finger, with escape of the thumb and index finger; slight disturbance of tactile sensation in the same parts with preservation of the sense of passive movement and of stereognosis; slight weakness shown especially in finer movements; sensation of coldness in the fingers although the surface temperature is normal, while in other cases there may be a sensation of warmth.

⁵⁸ *Revue Neurologique*, 1920, No. 3, p. 225.

Atrophy of the hand muscles and sympathetic oculopupillary signs have not been observed.

Barré and Schrapf believes these disturbances are all of sympathetic origin. Claude Bernard showed that the vasomotor fibers of the upper limbs are derived from the spinal cord as low as the seventh thoracic segment. Langley believed the greater part of the sympathetic fibers of these limbs come from the fourth to the tenth thoracic segments. Barré and Schrapf believe that the sympathetic fibers coming from the sixth to the eleventh thoracic segments supply the little and ring fingers especially, *i. e.*, the distribution of the ulnar nerve.

These same disturbances may be observed in visceral disease, especially affecting the base of the heart and aorta. They may be the first signs of lesion of the spinal cord and precede a paraplegia, as in Pott's disease or tumor of the cord, and may cause an incorrect diagnosis of the level of the lesion.

Spastic Spinal Monoplegia. Paralysis of one lower limb associated with atrophy, exaggerated tendon reflexes of the affected limb, and in some instances with spasticity, is a curious combination of symptoms. Cases of this kind have occurred in my⁵⁹ service at the University Hospital, Philadelphia, and similar cases have been reported by Sittig. The latter have been described in my review of the work of last year; but in Sittig's cases the upper limb was affected.

There is some danger that spastic monoplegia of cortical origin from a lesion of the cerebrum may be mistaken for one of spinal origin. Some of the cases of monoplegia with exaggeration of tendon reflexes result from injury of joint or bone in the affected limb or from the condition known by French writers as reflex paralysis. Where the bone or joint is affected there is likely to be pain, and spasticity is not conspicuous.

Even when the lesion is one of the spinal cord the spasticity may be slight. The explanation which appeals to me for the spastic spinal monoplegia is degeneration of both pyramidal tract and anterior horn of the spinal cord, a lesion similar to that of amyotrophic lateral sclerosis.

Absence of Pain in Tumor of the Gasserian Ganglion. Sicard has thought that the absence of pain in the face with anesthesia of the trigeminal nerve supply could be used in distinguishing a retroganglionic location of the lesion from one in the Gasserian ganglion. Implication of the sensory root he thought gave little or no pain. Marie, Bourtier and Bertrand⁶⁰ have reported a case in which this ganglion was destroyed by a tumor and yet no pain had been experienced. Usually the pain from such a lesion is very severe.

Persistence of Pain in Tic Douloureux. It seems to be of great importance whether the pain of tic douloureux is continuous or discontinuous. Sicard, Robineau and Paraf⁶¹ believe the local use of alcohol or the operation on the branches of the trigeminal nerve, its ganglion or sensory root is useless and even harmful in increasing the pain in all cases of continuous tic douloureux, but is sure to be successful in true trifacial

⁵⁹ Archives of Neurology and Psychiatry, 1920, No. 6, iii, 609.

⁶⁰ Revue Neurologique, 1920, No. 10, p. 977.

⁶¹ Ibid., 1921, No. 1, p. 82.

neuralgia where the pain is discontinuous. Gasserectomy, or better, the retrogasserian radicotomy more easily executed and less dangerous is always likely to give complete relief. The cessation of pain after the use of alcohol may be for five or ten years and only exceptionally permanent.

Continuity of pain in tic douloureux implies considerable implication of the sympathetic system, whereas discontinuity of pain is characteristic of the implication of a cranial or spinal nerve. Under this hypothesis one of their patients with tic douloureux was operated upon by cervical sympathectomy with removal of the superior and middle sympathetic ganglia, and yet the therapeutic result was *nil*, the pain persisted with its previous intensity.

Lhermitte does not believe persistent pain after any treatment indicates sympathetic involvement, there is a psychological factor which should not be ignored. The persistence of pain in certain cases of tic douloureux may be from involvement of the central sensory system, as pain of thalamic origin may be without any objective disturbance of sensation.

Neuritis of the Motor Branch of the Trigeminal Nerve. The paralysis of the motor part of this nerve without implication of other cranial nerves is rare, and especially is this so in the form described by Krabbe.⁶² A young man developed paralysis of the right motor fifth nerve during the epidemic of influenza, and atrophy developed gradually in the right temporal and masseter muscles, and yet objective sensation was normal in the right side of the face, but the right corneal reflex was a little diminished, otherwise the right sensory fifth nerve escaped.

Krabbe dismisses the theory that the paralysis may have been part of a poliomyelitis, because it developed during the influenza without paralysis of the limbs, or of the throat, or of the ocular muscles, or of other part of the face. There was no indication of syphilis.

Resection of the Sensory Root of the Trigeminal Nerve with Integrity of the Motor Root. It has been considered impossible to resect the sensory root of the trigeminal nerve and leave the motor root intact, but Frazier⁶³ has been able to accomplish this by the use of the electrode. The motor root when exposed he finds can positively be identified as motor by observing the temporal muscle contract. The directions he gives for this important operation are these:

When the sensory root is adequately exposed, in the course of the operation, it is elevated from its bed with a blunt instrument. Usually the motor root may be seen in contact with the skull traversing the space behind the root and disappearing behind the ganglion. If recognized or suspected, the electrode is applied; and should it prove to be the motor root, the fibers of the temporal muscle, exposed to view in the wound, will contract. Sometimes at this preliminary inspection the motor root will not be seen because, cleaving to the sensory root, it has been lifted up by the instrument with the sensory root. Under these circumstances he makes segmental sections of the sensory root, beginning with the outer fasciculi, and searches for the motor root after each

⁶² Revue Neurologique, 1920, No. 3, p. 241.

⁶³ Journal of the American Medical Association, January 8, 1921, p. 107.

section. Usually when half of the sensory root has been divided, one can recognize the motor root as it passes behind the ganglion. But to confirm the observation, the electrode is used. If these directions are followed, the motor root may be conserved in the majority of instances. It has escaped him occasionally, but with continued effort and experience he believes it will be possible to save the root in every instance.

With this refinement in technic, the radical operation might be said to be beyond criticism. Symmetry of the face is conserved, as there is no atrophy of the temporal muscle; there is no deviation of the jaw, since the pterygoid muscles are intact; and mastication is in no way interfered with.

Optic Neuritis Caused by Dental Sepsis. It is sometimes very difficult to find a cause for optic neuritis, and it is important to know that it may result from an abscess on a tooth. Archer-Hall⁶⁴ on March 8, 1920, examined a woman who complained of rapid loss of vision in the left eye and pain across the forehead, both of one week's duration. Vision was much impaired. The left fundus showed a typical optic neuritis, the disk was almost completely obscured, and the vessels, particularly the venules were very engorged. On the left side there was a carious upper molar whose crown was almost completely eroded. The patient did not complain of pain in this tooth but its removal was advised.

Two weeks later the optic neuritis had diminished and the visual acuity of the left eye had improved. The carious upper molar had been extracted, and at each of the three roots an abscess was found.

When examined nearly a month later the fundus was almost normal and the vision of the left eye with correction was almost normal. The case is interesting, as Archer-Hall says, first as an example of optic neuritis caused by neighboring sepsis, and secondly, on account of the rapid improvement with recovery of vision which followed removal of the foci of toxic absorption.

Thrombosis of the Subclavian Vein. This form of vascular obstruction is not very common, but George Wilson⁶⁵ has reported 2 cases in which it was the cause of severe brachial palsy. It is probably merely a coincidence that both patients were colored men. One man was tuberculous and died, but considerable recovery of function occurred in the second case.

Postdiphtheritic Paralysis of the Respiratory Muscles. Marriott⁶⁶ speaks of the paralyses following diphtheria as essentially temporary in character and as followed by complete restoration of function within a relatively short period of time. When there is extensive involvement of the respiratory muscles, death by suffocation is very likely to occur before recovery from the paralysis has taken place. An additional factor rendering the prognosis more grave is the myocardial involvement so frequently present coincident with the multiple neuritis. Respiratory difficulties of a mechanical nature serve further to embarrass the damaged heart.

⁶⁴ British Medical Journal, September 11, 1920, p. 399.

⁶⁵ Archives of Neurology and Psychiatry, January, 1921, No. 1, v, 109.

⁶⁶ Journal of the American Medical Association, September 4, 1920, p. 668.

Marriott states that if in the case of a patient suffering from these serious sequelæ of diphtheria, the respirations could be maintained by artificial means until the respiratory muscles had once more regained their function, one of the possible causes of death would be eliminated and the danger of death from cardiac failure somewhat minimized.

He reports a case which demonstrates the practicability of applying artificial respiration more or less continuously for a long period of time to a patient suffering from paralysis of the muscles of respiration. A child developed this form of paralysis following diphtheria, and it was evident that death from suffocation would result within a short time unless some means of artificial respiration were employed. An apparatus was employed designed to convert a continuous air current into an intermittent one of any desired rate and volume and used in physiologic laboratories. The artificial respiration was kept up at intervals for five days, and at the end of that time the respiratory muscles had so far regained their function, that the artificial respiration was necessary only at relatively infrequent intervals. Complete recovery occurred.

Results of Secondary Suture of Peripheral Nerves. According to Stopford,⁶⁷ if the suture has been deferred because of the presence of sepsis, widespread intraneural changes are likely to be encountered which will interfere seriously with, or prevent, regeneration. Excluding such a condition, a delay of twelve to eighteen months appears to have no marked effect upon the date or extent of recovery. If the interval exceeds this time, the prognosis is not so good when the suture has been performed in the distal part of the limb; whereas, in the proximal part, a delay of two or three years does not seem to prejudice the chances of success. Suture of the median in the upper arm he has found to be successful in two patients where there was an interval of two and a half years.

Complete solution of continuity is more favorable for suture than incomplete solution, but the difference is much reduced when a liberal resection is performed. Interstitial changes are frequently very extensive after partial division. Free resection is particularly necessary after prolonged suppuration. In none of his cases of secondary suture was the result perfect; in the best there was an appreciable difference in power on comparing the two sides. The recovery of sensation was particularly disappointing. More successful results have followed suture in the proximal part of the limb than the distal. For obvious reasons, muscles which have a large nerve of supply have a better chance than those in which the branch is smaller. The result which follows suture of the median and ulnar is usually poor. While the muscles have recovered voluntary power the hand is of slight practical service when the patient attempts purposive movements, and may be useful only when he concentrates upon it and watches its action. This disability is caused by the loss of afferent stimuli from joints, muscles, tendons and other deep structures.

Peripheral Neuritis Among Troops. Multiple neuritis was very common among British troops in Egypt and Palestine during the war and post-

⁶⁷ Brain, vol. xliii, Part I, p. 1.

diphtheritic paralysis formed the bulk of the cases in Walshe's⁶⁸ experience. He saw over 160 cases of the diphtheritic form. They were in two groups: The first consisting of the ordinary type following faucial diphtheria; the second, and in some ways the more interesting group, associated with extrafaucial infections of superficial skin lesions and of wounds by the diphtheria bacillus. Walshe, contrary to expectation, found that diminution and abolition of the knee and ankle jerks were by no means the initial signs of the malady. Subjectively, aching pains in the legs on exertion, painful cramps in the calves during the night, numbness of the feet and, objectively, tenderness of the calf and plantar muscles on pressure, with a remarkable facility of the tendon jerks, were the earliest phenomena. In 6 cases he observed that the knee and ankle jerks underwent a definite preliminary exaltation before they began to grow sluggish.

Cases of a mild type of multiple neuritis appeared without a history of sore throat or other evidence of faucial diphtheria, but associated with peculiar "septic sores" of the skin. The possibility of a secondary diphtheritic infection of the skin lesions was thought of, but at first this idea was dismissed because the multiple neuritis was neither preceded nor accompanied by palatal or accommodation paralysis. The septic sore was a condition in which small areas of superficial ulceration appeared upon the dorsum of the hand, the extensor surface of the forearm and on exposed parts of the leg around the knee. These were later recognized as diphtheritic and the bacillus was obtained from them.

Philip Manson-Bahr, in discussing Walshe's paper, described the sore as follows: The onset is sudden and very painful, out of proportion to the size of the lesion; within a few hours a vesicle forms filled with serous or hemorrhagic fluid, collecting generally around a hair follicle. The vesicle soon bursts and leaves behind a raw area generally covered with a pearly gray membrane and moist with exuding serum. The edges of the skin soon become undermined, and the ulcer spreads in a peripheral direction and soon becomes punched out, chronic, and most intractable. The effect of injection of 4000 units of antidiphtheritic serum in the neighborhood of these sores was said to be almost magical; raw patches and ulcers which had persisted for months or even years after treatment with every form of antiseptic lotion and paste, healed perfectly with sound, firm skin within a week or ten days.

Family Form of Musculospiral Palsy. It has been recognized for a long time that there may be a family form of paralysis of the facial nerve, as Kurt Mendel⁶⁹ points out, and it has been thought possible that the Fallopian canal in which the nerve lies may be unusually narrow in certain families. No mention is made in medical literature of any other form of nerve palsy occurring in several members of a family.

Mendel, however, has observed musculospiral palsy in a father and his two sons, and probably in two of the three it was from pressure, and yet in all 3 cases the cause was trivial. Mendel believed there must be a peculiar vulnerability of the nerve in this family, and he thinks there may be a similar vulnerability of the facial nerve in certain families.

⁶⁸ Brain, vol. xliii, Part I, p. 74.

⁶⁹ Neurologisches Centralblatt, January 16, 1920, p. 58.

Resection of the Pneumogastric and Glossopharyngeal Nerves for Pain. Pain in the soft palate, tonsil and pharynx may sometimes be intense, as in 3 cases reported by Sicard and Robineau.⁷⁰ One of these writers observed 2 cases in 1916 and 1917 in which pain was localized in the area mentioned, in 1 case on the right side and in the other on the left, without known etiology, without syphilitic infection, and without cure by antisiphilitic treatment. The pain occurred in attacks many times during the day and night, sometimes spontaneously, sometimes from deglutition, speaking or chewing. The pain was so severe as to produce a desire for suicide.

It was not possible to use alcoholic injection and resection was proposed, *viz.*, of the glossopharyngeus and the pharyngeal branches of the vagus, with removal of the superior cervical sympathetic ganglion, as the sympathetic is believed to have a role in the production of pain. The operation removed all pain, but 1 patient had a persistent paralysis of one vocal cord and the other atrophy of one side of the tongue.

The third case was without complicating paralysis other than that to be expected, except a paresis of one vocal cord which seemed to be disappearing. These authors therefore recommend this operation in suitable cases. It seems to be rather a formidable one, however.

Extracranial Paralysis of the Last Four Cranial Nerves. These lesions have been observed rarely before the war, but they cannot be said to have been common even during the war. Various names have been given depending on the combination of nerves affected. Pollock⁷¹ has observed 5 cases in which the last 4 cranial nerves were paralyzed, but the records of only 3 are available. As an illustration of the syndrome I refer to his case 1. A man was shot 1½ inches to the left of the fourth cervical spine, and had the wound of exit half an inch below the anterior extremity of the left zygomatic arch. He was hoarse, had difficulty in swallowing, marked salivation and dyspnea. He had a peripheral paresis of the left seventh nerve in addition. The posterior wall of the pharynx was pulled toward the right, especially when the tongue was pulled forward. No disturbance of taste could be demonstrated. Sensation over the left side of the soft palate was diminished. The left side of the soft palate was paralyzed, and the soft palate was pulled to the right, and in phonation this deviation was increased. There was some regurgitation of fluids. The gag reflex was absent on the left. The left vocal cord was paralyzed and the voice was hoarse and nasal. The sternocleidomastoid and trapezius muscles were paralyzed. The left hypoglossal nerve was paralyzed.

In this case there was evidently an extracranial injury of the ninth, tenth, eleventh and twelfth cranial nerves and a partial lesion of the seventh.

Grippe Neuritis. Paralysis of the abdominal muscles, more intense on the left side, occurring after the grippe is fortunately a rare occurrence but has been observed by Moreau,⁷² and at the time of the report there had been no improvement.

⁷⁰ Revue Neurologique, 1920, No. 3, p. 256.

⁷¹ Archives of Neurology and Psychiatry, 1920, iv, 517.

⁷² Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris, 36th Year, 1920, p. 81.

Alternating Facial Palsy. The occurrence of two attacks of peripheral facial palsy in the same person is not very rare. Remak found it in 6 out of 200 cases, or 3 per cent, Waterman in 335 cases found it in 2.7 per cent, but Petit and Bernhardt put the figures at 6 and 7 per cent respectively. Three attacks of peripheral facial palsy are much less common, and four attacks are said by Kurt Boas⁷³ to have been reported in only 5 cases in the literature. Five attacks have been observed only in 1 case. (Eulenburg). To these statistics Boas adds the report of a case in which four attacks occurred. He distinguishes the alternating form from the recurrent form, the first is that in which the same side of the face is not always affected. It is more common in males than in females, and the first attack is usually in childhood. Boas believes the recurrence is caused by unusual vulnerability of the facial nerve rather than by narrowness of the Fallopiian canal.

Treatment of Occipital Neuralgia. Pain in the distribution of the occipitalis major nerve may be severe and is to be treated much as is the pain in the distribution of the trigeminal nerve. Oehlecher⁷⁴ has had a considerable experience. He states that from 9 operated cases he believes evidence has been obtained to show that extirpation of the second spinal ganglion accomplishes what extirpation of the Gasserian ganglion accomplishes for trigeminal neuralgia. When the operation is undertaken the ganglion should be removed with the nerve. Recurrence of pain will not then occur, whereas if the occipital nerve should be removed without the ganglion, later removal of the ganglion would be very difficult. The removal of the ganglion is not an easy operation.

Local Paralysis Following Superficial Injuries (Reflex Paralysis.) As Walshe⁷⁵ puts it: among the many difficult problems confronting the neurologist a small group of cases of local paralysis after injury to a limb must be included, in which no nerve trunk has been involved. These cases present the features of an organic peripheral nerve lesion, and commonly follow a trivial superficial injury to the distal extremity of a limb. In seeking for an explanation of these two possible causes are advanced by Walshe: they are "reflex paralysis" and traumatic "ascending neuritis."

The reflex paralysis was once more popular than it is now, and was attributed to irritation of sensory nerve endings in the skin or viscera, but aside from the condition known as arthritic muscular atrophy a reflex paralysis was scarcely recognized until revived by Babinski. In joint disease it is common to have rapidly developing atrophy, weakness and exaggerated tendon reflexes of the affected limb, and the weakness is the result of the atrophy.

Babinski elaborated during the war a comprehensive symptom-complex of reflex nervous disorders, for which, as Walshe says, he seems to have drawn largely upon phenomena hitherto widely regarded as hysterical in nature. Within its limits he has included many gross objective signs of nervous disorder: wasting and loss of power, hypotonus and

⁷³ *Neurologisches Centralblatt*, September 1, 1920, p. 567.

⁷⁴ *Deutsche Zeitschrift für Nervenheilkunde*, 1921, vol. lxxviii and lxxix, p. 296.

⁷⁵ *Brain*, 1919, xlii, Part IV, p. 339.

contracture, exaggeration of tendon jerks with loss of cutaneous reflexes, altered mechanical and electrical excitability of muscles, trophic and vasomotor disorders, and marked subjective and objective sensory changes. These occur in various combinations and give rise to different clinical forms. Babinski terms these phenomena *physiopathic*, intending to express the idea that, on the one hand, neither hysteria nor any other psychopathic state can produce them, and, on the other hand, that while indicating a physical and material disorder of the nervous system they do not appear generally to correspond to any nervous lesion that can be detected by the methods at our disposal; they also tend to spread beyond the limits of any anatomical area.

Much doubt has been expressed as to whether these symptoms are the manifestations of a true clinical entity, and not rather that of a medley of abnormal conditions, to which hysteria, the mechanical effects of secondary tissue changes and even local tetanus may contribute their share. Walshe thinks that cases like those he describes may have helped to swell the numbers of this apparently ill-defined and heterogeneous collection of clinical forms that Babinski has named "reflex nervous disorders."

One alternative offered by Walshe is that possibly his own cases belong to the rare nervous affection known as "ascending neuritis." This diagnosis is very seldom made now, although the literature contains some examples, even in recent years, especially the French, English and German writers have been very skeptical of its occurrence. The pathological basis of this clinical complex is very doubtful, but Walshe believes it is not the lymphogenous toxi-infective process described by Orr and Rows. He says obscurity pervades the whole subject on both clinical and pathological sides. He reports 4 remarkable cases. In one a small suppurating wound of the dorsum of the foot was followed by paralysis of all the muscles supplied by the external popliteal nerve, and corresponding sensory loss. In another a superficial wound of the lower third of the thigh was followed by paresis and wasting of the quadriceps extensor femoris and diminution of the knee jerk. In another similar symptoms developed after a blow on the heel without a wound.

Walshe cannot explain his cases satisfactorily, as there is no sound pathology of these clinical conditions. They indicate that in rare instances the clinical manifestations of a local neuritis may follow trivial injuries, commonly associated with organismal infection, of the afferent terminations of the nerve affected.

In my article in *PROGRESSIVE MEDICINE* of September, 1918, under the name Reflex Paralysis I gave a digest of Mirallié's presentation of this extraordinary condition which has interested and puzzled many. One of the most illuminating papers on this subject is by Roussy.⁷⁶ He says the syndrome is characterized by contractures resulting in fixation of the larger articulations (hips, shoulders, elbows and knees) in defective postures, and by motor difficulties of a special type—contraction, paralysis or an association of both—localized in the distal ends of the limbs

⁷⁶ Archives of Neurology and Psychiatry, No. 3, vol. iv, p. 247.

and producing a condition described by the French as "main figée" (palsied stiff hand) and "pied bot réflexe" (reflex club foot).

Following a nervous shock caused by the bursting of a shell in close proximity, or traumatism, often slight, or certain other causes, a state of impotency, dependent on a more or less well developed pithiatic character, becomes manifest. The term "pithiatic" was introduced by Babinski and expresses his conception of hysteria. At the end of a period of time, which varies in the different cases, the influence of immobility or defective function, somewhat conditional on certain predispositions (circulatory, etc.) leads to secondary organic accidents, lasting as long as the immobility itself; these, however, gradually decrease and eventually disappear after an indefinite length of time, if the normal movements are restored.

The condition is one of hysterogenic associations. Two elements of the problem are to be considered: (1) The chief motor disorder; (2) the secondary disorders (vasomotor, trophic, etc.), which develop later.

The secondary disorders in the condition known as "stiffened hands" may be of many varieties. Vasomotor and thermic disorders may show by the skin of the hand and sometimes of the forearm becoming cyanotic, the color varying from bluish or purple to salmon red. The surface temperature may be lower than that of the normal hand. It may be shown by a sphygmomanometer that the arterial oscillations, especially during cold weather, are less in amplitude on the affected side; but after immersion in warm water the affected hand becomes warmer, and the arterial oscillations are of greater amplitude than on the healthy side. Observation will show that there are more or less obvious vasomotor disturbances in the healthy side, showing that those persons who develop "stiffened hands" do not possess a vasomotor system which functions normally, possibly on account of a congenital predisposition, and that the marked changes on the affected side are more easily produced by factors dependent on immobility than in normal persons.

The muscular contraction produced by tapping the muscles of the hand or arm with the finger is stronger and of longer duration on the affected side than on the healthy side. The electrical excitability of the muscle and nerves may be modified likewise, although a reaction of degeneration is never present.

Hyperhidrosis is often present on the affected side, sometimes so marked as to produce sudamina, but this disorder exists in persons in whom a tendency to excessive sweating is present also on the normal side.

Trophic disturbances are often marked. The skin becomes thin, smooth and glossy. The wrinkles are obliterated. When the vicious attitudes are of long duration, genuine cutaneous retractions may occur. The skin may be infiltrated and "succulent." The nails become hard, brittle and show transverse or longitudinal striations. Occasionally they are convex and deformed. They often grow faster than on the normal side. The hair is longer and thicker than on the normal side, or on the contrary, broken, smaller and less abundant.

Some muscular atrophy, generally slight, may occur. Tendinous

contractures are often present in long standing cases. The phalangeal and metacarpophalangeal articulations are frequently stiff and painful and at times even fibro-ankylosis is present. Nodular deformities, such as are found in arthritis, may occur. Even the bones may be so altered that decalcification and osteoporosis are revealed by roentgen-ray examination.

The tendon reflexes may be exaggerated on the affected side, and this increased excitability becomes even more pronounced when the patient is under chloroform. Muscular hypotonicity may be so marked in certain instances that the palmar surfaces of the fingers may touch the anterior surface of the forearm.

The description of the association of the motor disorders with the secondary disorders described above applies especially to the hand but similar conditions may occur with psychoneurotic contractures of the elbows, knees, hips and shoulders.

It is not surprising that the occurrence of paralysis of a part associated with such striking disorders as those described, and resulting from a trivial wound, or the bursting of a shell without apparent injury, should be difficult to explain. Are they hysterical or organic? This question, as Roussy says, was often discussed during the war and has not been unanimously and finally answered. Several theories have been advanced.

The reflex theory: The origin of these disorders is attributed to reflex causes, to changes in the nerve cells, of which the best known example is the arthritic muscular atrophy.

The dynamogenic theory: This includes the above but the reflex mechanism plays only a short and transitory role. If treated properly, the disorders will disappear without leaving any residuum, but if not so treated, the conditions become fixed by a psychic mechanism, and their constant presence produces dynamic modifications of the nervous centers as shown by the study of motor, sensory and reflex phenomena during the narcotic state.

The dyskinetic theory: This is a theory advanced by Roussy in association with Boisseau and d'Oelsnitz, and is supported by the careful clinical observations of more than 2000 cases of war psychoneuroses. Surely such a material as this commands respectful attention.

1. The motor disorder, contraction or paralysis, is the principal and primary element of the syndrome: it is also pithiatic (hysterical) in character and consequently capable of reproduction at the will of the patient. It is liable to disappear suddenly under the influence of persuasion if this method is employed under favorable conditions.

2. The associated disorders, which are commonly but not constantly present, are variable in character and very persistent. They are, according to Babinski's conceptions, comparable in every way to disorders admittedly hysterical in character. They are functional conditions that have appeared suddenly in patients predisposed to pithiatic motor disturbances. The origin of these secondary disorders is doubly conditional and dependent: (1) On elements of constitutional or acquired predisposition antedating the pithiatic motor disturbances, and, (2) on

determining causes operating for a longer or shorter time on an adequate predisposition and producing completely the array of secondary disorders. The most plausible hypothesis, according to Roussy, is that the full development of the secondary syndrome observed on the affected side is only an abnormal amplification of preëxisting tendencies observed on the healthy side. He believes that antalgic immobility through psychic inertia, following traumatism, as well as immobility obtained by compression in any fracture-reducing apparatus is enough to aggravate the preëxisting tendencies and cause secondary disorders to appear; and that later, the defective function of the limb promotes their progressive evolution and development.

The different disorders will occur in this chronological order: the caloric and vasomotor conditions with their sequelæ (mechanical hyperexcitability, modification of the electric reactions); the trophic disturbances, amyotrophias (with consequent hyperreflectivity), articular fibroankylosis and musculotendinous retraction. If immobility alone does not generally suffice to give rise to circulatory disorders which preëxist, it may, when associated with previous vasoconstriction, occasion them. Thus immobility and vasoconstriction, though of independent origin, are factors which undergo a parallel evolution and add their effects to produce the syndrome in its symptomatic whole.

When Roussy read his paper before the American Neurological Association he showed by moving pictures how he had induced a patient with a "stiffened hand" (*main figée*) to move this hand by making simultaneous movements with the sound hand like those he was attempting to make with the paralyzed hand. At first the paralyzed hand was hardly moved, but by repeated efforts under persuasion this hand gradually regained power, and after power was regained the very abnormal appearance disappeared. The presentation by Roussy seems to be a very convincing explanation of a very puzzling condition and worthy of the space I have given it.

Chorea. Pathological findings in Sydenham's chorea usually have not been satisfactory and have not explained the disease, so that a case carefully studied by Marie and Trétiakoff⁷⁷ arouses our interest. The duration of the disease in their case was ten days. They point out that the lesions of chorea are very similar to those of lethargic encephalitis, indeed they are said to differ only in the greater implication of the cerebral cortex in chorea; and they also mention that the differentiation clinically may also be difficult.

The lesions consist of mononuclear infiltration about the vessels and within the nervous tissues of the whole central nervous system except the medulla oblongata and cerebellum and are most intense in the basal ganglia. The gray matter is chiefly affected, the disease is a polioencephalitis, and the cerebral cortex is severely implicated. The findings are like those reported in similar cases by Méry and Babonneix, Delcourt and Sand, and some other recent investigators. There is a striking resemblance between these lesions found in Sydenham's chorea and those of Huntington's chorea.

⁷⁷ *Revue Neurologique*, 1920, No. 5, p. 428.

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